

# Bulletin Board

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**\* While Chemwatch has taken all efforts to ensure the accuracy of information in this publication, it is not intended to be comprehensive or to render advice. Websites rendered are subject to change.**

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## Regulatory Update

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### ASIA PACIFIC

#### Recent NZ EPA decisions

2024-09-09

##### Containment

APP204858 by Nufarm Limited to import or manufacture Nufarm containment approval for various experimental agricultural chemicals in containment. Approved with controls 27/08/2024.

APP204862 by Bayer New Zealand Limited to import or manufacture Bayer Trial Products 2024 (2) in containment. Approved with controls 23/08/2024.

##### Insecticide

APP204326 by Adama New Zealand Limited to import or manufacture Tekko Pro Insect Growth Regulator for release. Approved with controls 23/08/2024.

APP204706 by Renovo Technologies Ltd to import or manufacture RF-093 for release. Approved with controls 22/08/2024.

##### Fungicide

APP204549 by Syngenta Crop Protection Limited to import or manufacture INSTRATA Elite Turf Fungicide for release. Approved with controls 28/08/2024.

Read More

New Zealand EPA, 09-09-24

<https://www.epa.govt.nz/hazardous-substances/substance-approvals-and-group-standards/reassessments-and-changes-to-approvals/amended-approvals/>

#### Indonesia Accelerates Hydrogen Development As Key Clean Energy Source For Net Zero Target

2024-09-26

The Ministry of Energy and Mineral Resources (ESDM) is accelerating the development of hydrogen as a key component in Indonesia’s clean energy transition. In line with the country’s national hydrogen strategy, the ministry aims to position hydrogen as a crucial player in supporting



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renewable energy development, achieving decarbonization goals, and boosting Indonesia's potential as a global exporter of hydrogen.

Eniya Listiani Dewi, Director General of New, Renewable Energy, and Energy Conservation (EBTKE), outlined the Ministry's projections for hydrogen demand to reach 9.9 million tons per year (Mtpa) by 2060. The demand will come from various sectors, including industry, transportation, electricity, and household gas networks. Hydrogen will play a strategic role in Indonesia's efforts to achieve its Net Zero Emissions (NZE) target by 2060, or sooner.

"Hydrogen is a vital component in reducing carbon emissions, and establishing a specific KBLI (Standard Classification of Business Fields) for hydrogen will encourage innovation, investment, and collaboration across sectors," said Eniya during a public consultation on the matter. She emphasized that ensuring the economic viability and sustainability of hydrogen, particularly green hydrogen, is critical to Indonesia's energy transition.

Read More

Greenlear, 26-09-24

<https://www.gleaf.in/news/indonesia-accelerates-hydrogen-development-as-key-clean-energy-source-for-net-zero-target>

### Medsafe updating advice on nitrous oxide abuse

2024-09-22

Medsafe has been exploring regulatory options to address increasing misuse of nitrous oxide, leading to the decision to update its advice on the law in relation to the supply and use of nitrous oxide for recreational use.

Medsafe now advises that when nitrous oxide is sold primarily for the purpose of inducing a psychoactive effect, the Psychoactive Substances Act 2013 applies.

No products containing nitrous oxide have been approved for use under the Psychoactive Substances Act. It is illegal to sell nitrous oxide or products containing nitrous oxide for recreational use primarily to induce a psychoactive effect.

People who sell, offer to sell, or possess to sell nitrous oxide for recreational use are liable to penalties on conviction of up to two years

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imprisonment for an individual, or a fine of up to \$500,000 for a company, under section 70 of the Psychoactive Substances Act 2013.

An individual found to have an unapproved psychoactive substance, such as nitrous oxide, in their possession are liable to a penalty on conviction of a fine of up to \$500 under section 71 of the Psychoactive Substances Act 2013.

Previously, sales of nitrous oxide for recreational use have been considered to be selling a medicine without a prescription, as nitrous oxide is considered a medicine when used for inhalation for therapeutic purposes. However, in response to growing concern, Medsafe has reconsidered its position and now considers that recreational use is regulated under the Psychoactive Substances Act 2013.

Read More

NZ Ministry of Health, 22-09-24

<https://www.health.govt.nz/news/medsafe-updating-advice-on-nitrous-oxide-abuse>

## AMERICA

### Pregnant women exposed to PFAS may be at risk for obesity, heart disease later in life

2024-09-05

Women with higher levels of per- and polyfluoroalkyl substances (PFAS) during pregnancy may experience long-term weight gain and heart problems later in life, according to new research published in The Journal of Clinical Endocrinology & Metabolism.

PFAS are manmade chemicals found in food packaging, cookware, clothes, drinking water, personal care products and many other consumer goods. These endocrine-disrupting chemicals (EDCs) can interfere with hormones and cause health issues such as obesity, infertility and cancer.

"Our study supports the idea that pregnancy may be a sensitive period of PFAS exposure as it may be associated with long-term weight gain and subsequent adverse cardiometabolic health outcomes in women," said the study's first author Jordan Burdeau, Ph.D., of the Harvard T.H. Chan School of Public Health in Boston, Mass. "Our findings may improve understanding of the effects of PFAS on cardiometabolic health during



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pregnancy, which in turn may improve early prevention or detection of adverse cardiometabolic health outcomes in women.”

The researchers studied 547 pregnant women in their early 30s, comparing their PFAS levels during pregnancy with cardiometabolic health outcomes at age 50. They found women with higher levels of PFAS in their blood during early pregnancy weighed more and had more body fat at 50 years old than those with lower levels, potentially making them more susceptible to obesity and heart health problems later in life.

Read More

Endocrine Society, 05-09-24

<https://www.endocrine.org/news-and-advocacy/news-room/2024/pregnant-women-exposed-to-pfas-may-be-at-risk-for-obesity-heart-disease-later-in-life>

### Court Finds Typical Levels of Drinking Water Fluoridation Present an Unreasonable Risk to Health, Directs EPA to Take Regulatory Action

2024-09-30

After the U.S. Environmental Protection Agency (EPA) denied a 2016 petition filed under Section 21 of the Toxic Substances Control Act (TSCA) requesting that EPA consider whether fluoride in drinking water presents an unreasonable risk of injury to human health, a coalition of non-governmental organizations (NGO) promptly filed suit in the U.S. District Court for the Northern District of California. Food & Water Watch v. EPA (No. 3:17-cv-02162-EMC). After a bench trial in 2020, the court held the case in abeyance to wait for a final National Toxicology Program (NTP) Monograph that was issued in August 2024. On September 24, 2024, the court issued its decision, stating that the plaintiffs established by a preponderance of the evidence that the levels of fluoride typical in drinking water in the United States pose an unreasonable risk of injury to the health of the public. The court found that “fluoridation of water at 0.7 milligrams per liter (‘mg/L’) — the level presently considered ‘optimal’ in the United States — poses an unreasonable risk of reduced IQ in children.” The court notes that its finding “does not conclude with certainty that fluoridated water is injurious to public health; rather, as required by the Amended TSCA, the Court finds there is an unreasonable risk of such injury, a risk sufficient to require the EPA to engage with a regulatory response.” The order does not dictate how EPA must respond, but states

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that “[o]ne thing the EPA cannot do, however, in the face of this Court’s finding, is to ignore that risk.”

Read More

Law BC, 30-09-24

<https://www.lawbc.com/court-finds-typical-levels-of-drinking-water-fluoridation-present-an-unreasonable-risk-to-health-directs-epa-to-take-regulatory-action/>

### Safeguarding Our National Security with Practical PFAS Regulation

2024-10-01

Our country has made major environmental progress under the Biden-Harris administration. This is especially true as it relates to addressing exposure to a set of chemicals known as PFAS. The administration’s leadership was instrumental in negotiating and passing the Bipartisan Infrastructure Law, which appropriated over \$20 billion for detecting, treating, and reducing PFAS in public drinking water systems. President Biden and Vice President Harris also championed groundbreaking Environmental Protection Agency (EPA) regulations, including the establishment of the first national drinking water standard for PFAS, a ban on manufacturing inactive PFAS without EPA review, and the inclusion of additional PFAS into the Toxics Release Inventory. Their work will help safeguard the health and safety of communities and families right here in Arizona.

The EPA has a crucial responsibility to rigorously regulate PFAS as much as feasibly possible. The next step the agency is taking to discharge this responsibility is through a set of rules to develop effluent limit guidelines for PFAS. As the EPA produces these rules, it is vital that they balance the need to protect public health with the key role these substances play in U.S. manufacturing, particularly in relation to national security. New regulations must ensure continued access to PFAS for essential applications.

As a former law enforcement officer of 26 years for the City of Phoenix, School Safety Resource Officer (SRO) and a lifelong community advocate of affordable housing, Job Creation and the Economy, I recognize that the safety and well-being of our communities always comes first.



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Read More

Arizona Capitol Times, 01-10-24

<https://azcapitoltimes.com/news/2024/10/01/safeguarding-our-national-security-with-practical-pfas-regulation/>

### EUROPE

#### Nanotechnology – promoting uses of new assessment methods

2024-09-19

NAMs refers to a wide variety of methods for testing and assessing chemicals that do not use experiments on animals or humans. As well as gradually replacing animal testing, these methods can contribute to improved safety assessments by using models that better simulate conditions in humans.

NAMs can be performed in test tubes, culture dishes, or using software. NAM-based approaches offer great potential for assessing the safety of nanotechnology since in many cases traditional methods cannot easily be adapted to address nanoscale hazards. In particular, their use in the first steps of a risk assessment can minimise the need for additional animal studies.

Advances in science and technology are stimulating a flood of these approaches, however few of them have been validated according to international standards for use in regulatory risk assessments.

Read More

EFSA, 19-09-24

<https://www.efsa.europa.eu/en/news/nanotechnology-promoting-uses-new-assessment-methods>

#### Calls for EUDR postponement have created confusion for companies over when and if they will have to comply.

2024-09-30

As lawmakers clash this month over whether to stick with rigid enforcement of the EU's new Regulation on Deforestation-Free Products

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(EUDR), with obligations set to take effect in December, companies have been left questioning whether they should move forward with urgent reporting and certification preparation.

Earlier this month, German Food and Agriculture Minister Cem Özdemir asked the European Commission to postpone the regulation's application by six months to 1 July 2025, saying: "The Commission must finally come out of the summer break and provide clarity," he wrote. "I take the concerns of companies, agriculture and forestry, and the countries very seriously. Companies need sufficient time to prepare."

He added: "This also applies to countries with small-scale production structures. Otherwise, supply chains threaten to break at the end of the year - to the detriment of the German and European economy, small farmers in third countries, and consumers."

#### 'Bureaucratic monster'

The message has also been carried forward by conservative German members of the European Parliament. "We call on the Commission to immediately delay the implementation of the Deforestation Law," said Herbert Dorfmann, EPP coordinator in the European Parliament's Agriculture Committee, this week. Peter Liese, a powerful member of the Parliament's Environment Committee, agreed and called the legislation a "bureaucratic monster" which could threaten the EU's animal feed supply and disrupt trade in many consumer goods.

To calm growing alarm, the Commission said it would come out with additional guidelines in the Spring. But these guidelines have yet to emerge.

Centre-left MEPs are urging the Commission to stick to the original timeline for implementing the law. A group of centre-left MEPs, including Italy's Brando Benifei and Germany's Delara Burkhardt, have sent the Commission a letter saying, "It is crucial that the EUDR is applied without delay." They urged the Commission to quickly finalise the guidelines and FAQs as a matter of urgency and said a "user-friendly IT system" should be created for companies to submit compliance documents.

Read More

EURACTIV, 30-09-24

<https://www.euractiv.com/section/agriculture-food/news/eu-deforestation-law-in-doubt-as-germany-pushes-for-postponement/>



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### Italy calls for early review of EU combustion engine ban

2024-09-08

The European Union should decide already next year whether to rethink regulation that effectively bans the sale of new petrol and diesel cars in the 27-nation bloc from 2035, Italy's industry minister said on Saturday.

Speaking on the sideline of TEHA business forum in Cernobbio, Adolfo Urso said an intermediate assessment on the progress to meet the new rules, currently due in 2026, should instead take place at the beginning of next year.

"I think this should be the first issue the new European Commission deals with, because companies and workers need clarity", said Urso.

Agreed EU law will require new cars sold after 2035 to have zero carbon emissions, making it impossible to sell new fossil fuel-powered vehicles in the region.

The right-wing government of Giorgia Meloni believes the European Commission should allow member states to have more freedom in choosing the technology they prefer to meet agreed decarbonisation targets and supports a more gradual shift away from combustion engine technology.

Read More

Reuters, 08-09-24

<https://www.reuters.com/world/europe/italy-calls-early-review-eu-combustion-engine-ban-2024-09-07/>

## INTERNATIONAL

### Scientific reviewers from across globe encouraged to participate in landmark environmental report

2024-09-25

Since it was first published in 1997, the Global Environment Outlook has had an ambitious goal: assess the state of the planet and offer fixes to some of the Earth's most-pressing environmental challenges.

The seventh edition of the report, or GEO-7, is now in the works.

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Developed under the stewardship of the United Nations Environment Programme (UNEP), GEO-7 will focus on solutions to the triple planetary crisis of climate change, nature, land and biodiversity loss, and pollution and waste.

Underpinning the work of more than 250 authors writing the report are hundreds of technical reviewers. These subject-matter experts are tasked with determining if the report's findings are consistent with the latest science and identifying any information gaps that might exist.

Each chapter of the report goes through multiple rounds of review from experts around the world. Those involved say that it is important for making sure GEO-7 lives up to its mission of providing robust, peer-reviewed science that can guide policymaking globally.

"One of the most important things is to make sure that the reviewers represent a wide range of geographic backgrounds and areas of expertise," said Detlef Van Vuuren, climate scientist and GEO-7 author. "This ensures there are no blind spots during the review process."

Read More

UNEP, 25-09-24

<https://www.unep.org/news-and-stories/story/scientific-reviewers-across-globe-encouraged-participate-landmark>

### Elevating action on super pollutants for rapid climate gains

2024-09-26

Excellencies and colleagues. Welcome to this event on super pollutants. My thanks to Sir Andrew Steer for joining us as facilitator.

The climate crisis is intensifying, bringing death, destruction and economic damage across the world. Yet existing commitments under the Paris Agreement will see global temperatures far exceed 1.5°C. Unless we act with urgency, far worse is to come.

We know that super pollutants such as methane, black carbon, hydrofluorocarbons and tropospheric ozone cause around half of today's warming. And we know that firm action on these super pollutants can bring rapid gains. Put us on track for a cooler planet. Deliver action across the full triple planetary crisis – the crisis of climate change, the crisis of



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nature and biodiversity loss, and the crisis of pollution and waste. And, of course, bring benefits for human health and economies.

There are already many commitments on super pollutants, from the Global Methane Pledge to the Kigali Amendment to the Montreal Protocol. And a new report on nitrous oxide to be released at the upcoming meeting of the parties of the Montreal Protocol sheds light on another super pollutant that requires urgent attention.

Read More

UNEP, 26-09-24

<https://www.unep.org/news-and-stories/speech/elevating-action-super-pollutants-rapid-climate-gains>

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## REACH Update

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### Highlights from September RAC and SEAC meetings

2024-10-02

The Committees for Risk Assessment (RAC) and for Socio-Economic Analysis (SEAC) reached provisional conclusions on the proposed restriction of PFAS in the petroleum and mining sector. RAC also adopted its opinion on the harmonised classification and labelling of Talc, recommending carcinogenicity as the most stringent classification.

Helsinki, 26 September 2024 – In their September meetings, RAC and SEAC discussed the following sectors from the EU-wide proposal to restrict per- and polyfluoroalkyl substances (PFAS):

- Petroleum and mining;
- Textiles, upholstery, leather, apparel and carpets; and
- Food contact material and packaging.

The committees provisionally concluded on their evaluation of the petroleum and mining sector. Discussions on the other two sectors - textiles, upholstery, leather, apparel and carpets, and food contact material and packaging - will continue in the next meetings.

RAC agreed to revise how PFAS emissions are calculated across different sectors with a focus on the waste stage, for example emissions from waste disposal and incineration. The revised approach emphasises the need to distinguish between PFAS particle emissions (solid) and those that leach from materials. This distinction is important because the concerns related to fluoropolymer particles differ from those associated with non-polymeric PFAS.

The committees also announced the sectors they will evaluate in the upcoming meetings. In November, they will discuss construction products for the first time. After November, the next sectors for discussion are: Applications of fluorinated gases;

- Transport; and
- Energy.

Read More

ECHA, 02-10-24

<https://echa.europa.eu/-/highlights-from-september-2024-rac-and-seac-meetings>

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## REACH Update

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### Assessment of regulatory needs report published

2024-10-02

Report for the following substance group is now available on our website:

- Alpha amino acids and salts

If you have questions or feedback related to the assessment work, you can send them to us using this webform.

[Read More](#)

ECHA, 02-10-24

<https://echa.europa.eu/assessment-regulatory-needs>

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## Janet's Corner

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### Solution

2024-10-04



<https://www.calpaclab.com/science-jokes/>



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## Hazard Alert

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### Toluene

2023-10-04

Toluene occurs naturally in crude oil and in the tolu tree. It is also produced in the process of making gasoline and other fuels from crude oil and making coke from coal. [1,2]

### USES [2,3]

The majority of toluene is used as a component of petrol. It is also used in paints, lacquers, inks, adhesives, rubber, and cleaning agents. It is used to manufacture benzene, urethane raw materials, and other organic chemicals. It is used in the production of pharmaceuticals, dyes, and cosmetic nail products. It is used against roundworms and hookworms.

### EXPOSURE SOURCES & ROUTES OF EXPOSURE [3]

#### Exposure Sources

**Air:** Air pollution from motor vehicle exhaust is unquestionably a major source of exposure. Occupational subpopulations involved in toluene production or use are likely to be exposed to considerably higher levels than the general population. In addition, air levels in the vicinity of industrial sources and petrol stations are likely to represent an additional burden to both workers and local residents.

**Smoking:** Toluene is a major component of tobacco smoke and concentrations can vary greatly. The concentration per cigarette in sidestream smoke is typically higher than in mainstream smoke. The amount of toluene in mainstream smoke from an unfiltered cigarette was estimated to range from 100 to 200 mg with a sidestream/mainstream smoke ratio of 1.3, using samplers to adsorb toluene in the breathing zone of smokers and nonsmokers over a 24-hour period, found that active smokers were exposed to about four times the level for passive smokers. Cigarette smoking enhanced elimination of toluene and hippuric acid from the body. Smokers had significantly higher blood levels than nonsmokers with the level affected more by the length of time since the last cigarette was smoked than by the extent of smoking.

**Drinking-water:** Exposure via drinking-water is minor, except in cases of unusually heavy contamination. Levels indicated by surveys in the USA are generally less than 10 µg/l.

**Toluene, formerly known as toluol, is a clear, water-insoluble volatile liquid with an aromatic odour (smells like paint thinners) and the molecular formula C<sub>6</sub>H<sub>5</sub>CH<sub>3</sub>.**

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**Food:** Exposure via food is also considered to be insignificant. A daily contribution from fish was estimated to be between 0.1–0.2 mg/kg bw.

Inhalation is the predominant route of exposure.

### HEALTH EFFECTS [4]

#### Acute Health Effects

- The Central Nervous System (CNS) is the primary target organ for toluene toxicity in both humans and animals for acute and chronic exposures. CNS dysfunction (which is often reversible) and narcosis have been frequently observed in humans acutely exposed to low or moderate levels of toluene by inhalation; symptoms include fatigue, sleepiness, headaches, and nausea. CNS depression and death have occurred at higher levels of exposure. Cardiac arrhythmia has also been reported in humans acutely exposed to toluene. Following the ingestion of toluene a person died from a severe depression of the CNS. Constriction and necrosis of myocardial fibres, swollen liver, congestion and haemorrhage of the lungs, and tubular kidney necrosis were also reported. Acute exposure of animals to toluene has been reported to affect the CNS as well as to decrease resistance to respiratory infection. Acute animal tests in rats and mice have demonstrated toluene to have low acute toxicity by inhalation or oral exposure.

#### Carcinogenicity

- Available studies in workers have reported limited or no evidence of the carcinogenic potential of toluene. Similarly, the few available epidemiological studies have failed to demonstrate increased risk of cancer due to inhalation exposure to toluene. However, these studies were limited due to the size of the study population and lack of historical monitoring data.
- Chronic inhalation exposure of rats did not produce an increased incidence of treatment-related neoplastic lesions.
- Under the Guidelines for Carcinogen Risk Assessments (US. EPA, 2005), the EPA considers that there is inadequate information to assess the carcinogenic potential of toluene.



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### Other Effects

- CNS dysfunction, attention deficits, minor craniofacial and limb anomalies, and developmental delay were observed in the children of pregnant women exposed to toluene or to mixed solvents during solvent abuse. Growth retardation and dysmorphism were reported in infants of another study. However, these studies were confounded by exposure to multiple chemicals. Children born to toluene abusers have exhibited temporary renal tubular acidosis.
- Paternal exposure (in which the mothers had no occupational exposure to toluene but the fathers did) increased the odds ratio for spontaneous abortions; however, these observations cannot be clearly ascribed to toluene because of the small number of cases evaluated and the large number of confounding variables. An increased incidence of spontaneous abortions was also reported among occupationally exposed women. However, these studies are not conclusive due to many confounding variables.
- Several inhalation studies have shown toluene to be a developmental toxicant, but not a reproductive toxicant, in rodents.

### SAFETY

#### First Aid Measures [5]

- **Eye Contact:** Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Get medical attention.
- **Skin Contact:** In case of contact, immediately flush skin with plenty of water. Cover the irritated skin with an emollient. Remove contaminated clothing and shoes. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention.
- **Serious Skin Contact:** Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek immediate medical attention.
- **Inhalation:** If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.
- **Serious Inhalation:** Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. WARNING: It may

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be hazardous to the person providing aid to give mouth-to-mouth resuscitation when the inhaled material is toxic, infectious or corrosive. Seek medical attention.

- **Ingestion:** Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately. Loosen tight clothing such as a collar, tie, belt or waistband.

#### Workplace Controls & Practices [4]

- Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapours below their respective threshold limit value.
- Ensure that eyewash stations and safety showers are proximal to the work-station location.

#### Personal Protective Equipment [5]

The following personal protective equipment is recommended when handling toluene:

Splash goggles;

- Lab coat;
- Vapour respirator (be sure to use an approved/certified respirator or equivalent);
- Gloves.

Personal Protective Equipment in Case of a Large Spill:

Splash goggles;

- Full suit;
- Vapour respirator;
- Boots;
- Gloves;
- A self contained breathing apparatus should be used to avoid inhalation of the product.
- Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.



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REGULATION

United States

Exposure Limit	Limit Values	HE Code	Health Factors and Target Organs
<b>OSHA Permissible Exposure Limit (PEL) - General Industry</b> See 29 CFR 1910.1000 Table Z-2 (See also ANSI Z37.12-1967)	200 ppm TWA 300 ppm Ceiling 500 ppm Peak (10 minutes)	HE7	Central nervous system depression, causing fatigue, headache, confusion, paresthesia, dizziness, and muscular incoordination
		HE15	Irritation of the eyes, mucous membranes, and upper respiratory tract
<b>OSHA PEL - Construction Industry</b> See 29 CFR 1926.55 Appendix A	200 ppm (750 mg/m <sup>3</sup> ) TWA	HE7	Central nervous system depression, causing fatigue, headache, confusion, paresthesia, dizziness, and muscular incoordination
		HE15	Irritation of the eyes, mucous membranes, and upper respiratory tract

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Exposure Limit	Limit Values	HE Code	Health Factors and Target Organs
<b>OSHA PEL - Shipyard Employment</b> See 29 CFR 1915.1000 Table Z-Shipyards	200 ppm (750 mg/m <sup>3</sup> ) TWA	HE7	Central nervous system depression, causing fatigue, headache, confusion, paresthesia, dizziness, and muscular incoordination
		HE15	Irritation of the eyes, mucous membranes, and upper respiratory tract
<b>National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL)</b>	100 ppm (375 mg/m <sup>3</sup> ) TWA 150 ppm (560 mg/m <sup>3</sup> ) STEL	HE7	Fatigue, weakness, confusion, headache, dizziness, drowsiness
		HE8	Unconsciousness
		HE15	Irritation of the eyes, respiratory tract, and skin
<b>American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) (2007)</b>	20 ppm (75 mg/m <sup>3</sup> ) TWA A4; BEI	HE5	Female reproductive system damage and pregnancy loss
		HE7	Central nervous system impairment and visual impairment

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Exposure Limit	Limit Values	HE Code	Health Factors and Target Organs
CAL/OSHA PELs	10 ppm (37 mg/m <sup>3</sup> ) TWA	HE5	Female reproductive toxicity, spontaneous abortion
	500 ppm Ceiling 150 ppm (560 mg/m <sup>3</sup> ) STEL Skin	HE7	Impaired colour vision, impaired hearing, decreased performance in neurobehavioral analysis, changes in motor and sensory nerve conduction velocity, headache, and dizziness

The United States Environmental Protection Agency (EPA) has set a limit of 1 milligram per litre of drinking water (1mg/L).

- Discharges, releases, or spills of more than 1,000 pounds of toluene must be reported to the National Response Centre.

## REFERENCES

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"Functional cure" for diabetes restores insulin production with stem cells

2024-09-30

Type 1 diabetes is an autoimmune disease where the patient's immune system attacks insulin-producing cells in the pancreas. This means patients become unable to manage their blood glucose levels and require regular injections of insulin.

Now, early results from a phase I clinical trial suggest that replacing those lost insulin-producing cells with new ones could be a viable treatment. The first patient to receive this kind of transplant has now been insulin-independent for over a year, the team says.

The patient is a 25-year-old woman who was diagnosed with type 1 diabetes 11 years earlier. Since then, she'd been dependent on insulin treatment, and had undergone two liver transplants and a pancreas transplant as a result of her condition.

For the trial, the scientists isolated stem cells from her adipose tissue, and induced them to return to an earlier state of development, from which they could differentiate into almost any cell type. Then, they were coaxed to become pancreatic islet cells, which were cultivated and transplanted into her abdominal muscles.

The team monitored her closely for a year after the transplant. Her daily insulin dose requirements began to drop after two weeks, and by day 75 she was completely insulin independent. She remained that way for the rest of the one-year study period, spending over 98% of the time within a healthy glycemic range. The scientists report no indication of abnormalities from the transplant.

Other studies have been done before with similar promising results, but this new trial differs in a few key ways. For one, the stem cells are induced chemically rather than genetically, and come from a different source within the patient's body.

They were also implanted into the abdominal muscles rather than the liver like previous studies. This improved the survival and maturation of the cells, made them easier to monitor and was a less invasive procedure for the patient.

A potential complication is that the patient's immune system still needs to be suppressed – after all, replacing the damaged cells doesn't tackle the root cause of this autoimmune condition. But that's par for the course with organ and tissue transplantations.



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The trial shows that the treatment could be a viable option for diabetes, with further work. Currently, two other participants are enrolled in the trial,

The research was published in the journal Cell.

**Source:** Nankai University via Xinhua

New Atlas, 30 September 2024

<https://newatlas.com>

### Promising Lassa Fever Vaccine Prevents Disease and Death in Preclinical Animal Models

2024-09-13

Vaccine shows potential to prevent severe disease and death in animals.

Researchers from Thomas Jefferson University and the University of Maryland Baltimore, in collaboration with the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) and the Geneva Foundation, have developed a promising new vaccine candidate that protects against Lassa fever. The study, published in *npj Vaccines* on August 9, 2024, demonstrated that the vaccine effectively prevents severe cases of the disease and death in preclinical animal models and paves the way for research in people.

To date, several Lassa candidate vaccines are currently in development. However, out of these, Matthias Schnell, PhD, director of the Jefferson Center for Vaccines and Pandemic Preparedness at Thomas Jefferson University, who co-led the study, pointed out that his team's LASSARAB vaccine has an advantage. He noted that the two other platforms in development for Lassa fever are both based on live viral vectors, "which come with their own safety issues," he says. "Our vaccine is a deactivated or killed vaccine which is considered safer in general."

The vaccine, named LASSARAB, uses a deactivated rabies virus platform to deliver antigens to protect against the Lassa fever virus. Lassa fever is a severe hemorrhagic disease that is endemic to parts of West Africa, causing an estimated 300,000 to 500,000 infections and over 5,000 deaths each year. The disease can lead to severe complications including organ failure, deafness, and long-term neurological disorders. Currently, there are no licensed vaccines to prevent Lassa fever.

"The damage to a patient is devastating," says Kathleen Cashman, PhD, a virologist and principal investigator at The Geneva Foundation supporting

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USAMRIID who also co-led the study. She adds that the virus infects and compromises cells, causing multiple organ failures which can be fatal. "It is a very severe disease that's difficult to protect against, so when you find something that can keep you from dying, that's pretty astounding."

The researchers used 12 young non-human primates to test the vaccine, half receiving two doses of the LASSARAB vaccine, and the other half receiving CORAVAX, a COVID-19 vaccine, as a negative control. While both used rabies as a vector, the antigens used to activate an immune response were different. Over 28 days, the control group exhibited more severe disease symptoms, greater damage to their internal organs, and did not survive, while the LASSARAB-vaccinated group had less damage and survived until the end of the study. The researchers also noted that much remains unknown about the persistence of the disease in young animals in general, highlighting the need for further research.

While the vaccine protected against severe disease and death and reduced fever, it did not prevent infection. The researchers believe the 28-day study period was not long enough to fully assess the vaccine's ability to provide long-term immunity. They are optimistic that longer-term studies with more mature animal models will provide further insights into the vaccine's ability to prevent long-term side effects.

The rabies platform used in the LASSARAB vaccine was developed by Dr. Schnell's lab and offers several key advantages. In addition to protecting against Lassa fever, the vaccine also protects against rabies which is an important consideration for many Lassa-endemic regions. Previous studies have shown that a similar rabies-based vaccine against the Ebola virus can also remain stable at a variety of temperatures including 50 degrees Celsius for up to two weeks. Dr. Schnell, also chair of the Department of Microbiology and Immunology at Sidney Kimmel Medical College, highlighted that rabies vaccines have a proven safety profile, allowing for their use in children and immunosuppressed populations. This dual protection could be particularly beneficial in regions where both diseases are prevalent.

"If you get vaccinated and boosted against rabies, most people have lifelong protection," Dr. Schnell says. "So, we hope that the protection against Lassa will be also long-lived, which is important."

Funding for this study was provided by a \$30 million grant from the National Institute of Allergy and Infectious Diseases (NIAID), which has been crucial in advancing the vaccine candidate to this critical stage. "This kind of work needs government and nonprofit funding," says Dr. Schnell,



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who added that the team is very grateful to receive this funding since there are limited commercial incentives from pharmaceutical companies for this type of vaccine. "This is not a SARS-CoV-2 vaccine. This vaccine is for neglected infectious diseases in a region of poor financial standing, so these people need our help."

To that end, Dr. Schnell's Lassa virus vaccine is now headed to a phase 1 clinical trial in November after successfully completing an Investigational New Drug (IND) application with the Food and Drug Administration.

Techology Networks, 13 September 2024

<https://technologynetworks.com>

### New Research Says This "Healthy" Tea May Actually Cause Liver Damage

2024-09-30

Green tea is well-known for its health benefits, from preventing cancer, heart disease, and metabolic disorders to offering anti-inflammatory properties. As a result, it's become the second-most consumed beverage worldwide, with its popularity for weight loss on the rise.

However, the positive effects of green tea might not be the full picture. According to a December 2022 review article in *GastroHep*, green tea consumption could actually damage your liver health.

#### What to know about green tea

As the popularity of green tea continues to soar, Professor Stephen Malnick, lead author and head of the internal medicine department at Kaplan Medical Center, emphasizes the relevance of their recent publication. He points out that the green tea market in the United States could grow to an impressive \$27 billion by the end of this decade, showing just how much people love this healthy drink.

However, he reminds us that green tea can sometimes be a mix of materials from different countries, and some might contain tiny amounts of heavy metals, which can be bad for you. So always be sure to choose high-quality green tea from trusted sources.

Although uncommon, it's also important to note that according to the National Center for Complementary and Integrative Health (NCCIH – a division of the NIH), green tea extracts in pill form have been the main culprit in some individuals reporting liver problems.

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#### The positive effects of green tea

Brimming with antioxidants known as catechins, your cup of green tea boasts an impressive array of health advantages. These mighty catechins have been linked to cancer prevention, with studies indicating their potential to decrease the risk of breast, prostate, and colorectal cancers.

Green tea also enhances heart health by promoting better blood flow, reducing cholesterol levels, and preventing blood clot formation. And if that's not enough, green tea can rev up your metabolism and aid in fat burning, making it a go-to choice for weight loss or weight maintenance.

#### Green tea and liver health

While enjoying the numerous health benefits of green tea, you also need to be aware of potential liver-related side effects presented by the authors. Researchers at Israel's Clalit Health Service and Kaplan Medical Center examined case reports, studies focusing on specific amounts of tea from the same plants or plant mixes, and cellular and animal experiments to gain a comprehensive understanding of green tea's effect on liver health.

They found that botanical toxins in the tea plant may cause a metabolic reaction and lead to liver inflammation in some individuals. Green tea can also cause herbal-induced liver injury (HILI), an uncommon but potentially severe issue. With only 100 cases documented worldwide, HILI can result in acute liver failure or damage that takes months or years to reverse.

Diagnosing a direct connection between green tea consumption and liver failure can be challenging. It's also worth noting that the exact components responsible for liver damage are not yet clear, and combining green tea with other drugs and herbs can lead to severe liver disease in some people. Nonetheless, the authors stress the importance of staying informed about potential risks and consulting a healthcare professional if you experience any suspicious symptoms.

#### What to look out for when consuming green tea

Practicing moderation is crucial in green tea consumption, so stick to a reasonable amount, such as 2-3 cups per day, and avoid overconsumption. If you consider incorporating green tea into your daily routine, discuss it with your healthcare provider first. They can help you determine the right amount for your needs and ensure it doesn't interact with your medications.



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Finally, pay attention to your body: if you experience any symptoms, such as abdominal pain, jaundice (yellowing of the skin or eyes), or dark urine, after consuming excessive amounts of green tea, stop drinking it immediately and consult your healthcare provider.

The Healthy, 30 September 2024

<https://thehealthy.com>

### Manganese Cathodes Could Boost Lithium-Ion Batteries

2024-09-26

Manganese is abundant and cheap. A new process could make it a contender to replace nickel and cobalt in batteries.

Rechargeable lithium-ion batteries are growing in adoption, used in devices like smartphones and laptops, electric vehicles, and energy storage systems. But supplies of nickel and cobalt commonly used in the cathodes of these batteries are limited. New research led by the Department of Energy's Lawrence Berkeley National Laboratory (Berkeley Lab) opens up a potential low-cost, safe alternative in manganese, the fifth most abundant metal in the Earth's crust.

Researchers showed that manganese can be effectively used in emerging cathode materials called disordered rock salts, or DRX. Previous research suggested that to perform well, DRX materials had to be ground down to nanosized particles in an energy-intensive process. But the new study found that manganese-based cathodes can actually excel with particles that are about 1000 times larger than expected. The work was published Sept. 19 in the journal *Nature Nanotechnology*.

"There are many ways to generate power with renewable energy, but the importance lies in how you store it," said Han-Ming Hau, who researches battery technology as part of Berkeley Lab's Ceder Group and is a PhD student at UC Berkeley. "By applying our new approach, we can use a material that is both earth-abundant and low-cost, and that takes less energy and time to produce than some commercialized Li-ion battery cathode materials. And it can store as much energy and work just as well."

The researchers used a novel two-day process that first removes lithium ions from the cathode material and then heats it at low temperatures (about 200 degrees Celsius). This contrasts with the existing process for manganese-based DRX materials, which takes more than three weeks of treatment.

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Researchers used state-of-the-art electron microscopes to capture atomic-scale pictures of the manganese-based material in action. They found that after applying their process, the material formed a nanoscale semi-ordered structure that actually enhanced the battery performance, allowing it to densely store and deliver energy.

The team also used different techniques with X-rays to study how battery cycling causes chemical changes to manganese and oxygen at the macroscopic level. By studying how the manganese material behaves at different scales, the team opens up different methods for making manganese-based cathodes and insights into nano-engineering future battery materials.

"We now have a better understanding of the unique nanostructure of the material," Hau said, "and a synthesis process to cause this 'phase change' in the material that improves its electrochemical performance. It's an important step that pushes this material closer to battery applications in the real world."

This research used resources at three DOE Office of Science user facilities: the Advanced Light Source and Molecular Foundry (National Center for Electron Microscopy) at Berkeley Lab, and the National Synchrotron Light Source II at Brookhaven National Laboratory. The work was supported by DOE's Office of Energy Efficiency and Renewable Energy and Office of Science.

Technology Networks, 26 September 2024

<https://technologynetworks.com>

### Siloxane nanoparticles unlock precise organ targeting for mRNA therapy

2024-10-01

Penn Engineers have discovered a novel means of directing lipid nanoparticles (LNPs), the revolutionary molecules that delivered the COVID-19 vaccines, to target specific tissues, presaging a new era in personalized medicine and gene therapy.

While past research -- including at Penn Engineering -- has screened "libraries" of LNPs to find specific variants that target organs like the lungs, this approach is akin to trial and error. "We've never understood how the structure of one key component of the LNP, the ionizable lipid, determines



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the ultimate destination of LNPs to organs beyond the liver," says Michael J. Mitchell, Associate Professor in Bioengineering.

In a new paper published in *Nature Nanotechnology*, Mitchell's group describes how subtle adjustments to the chemical structure of the ionizable lipid, a key component of the LNP, allows for tissue-specific delivery, in particular to the liver, lungs and spleen.

The researchers' key insight was to incorporate siloxane composites, a class of silicon- and oxygen-based compounds already used in medical devices, cosmetics and drug delivery, into the ionizable lipids that give LNPs their name.

Much like silicon housewares, which are known for being durable and easy to sanitize, siloxane composites have been shown in prior research to have high stability and low toxicity. "We sought to explore if these attributes could be exploited to engineer highly stable and minimally toxic LNPs for mRNA delivery," the researchers report in the paper.

By carefully testing hundreds of variants of the newly christened siloxane-incorporating lipid nanoparticles (SiLNPs), the researchers determined which chemical features had an effect on mRNA delivery. "Identifying their in vivo delivery was a huge challenge," says Lulu Xue, a postdoctoral fellow in the Mitchell Lab and one of the paper's co-first authors.

At first, the researchers used the SiLNP variants to deliver mRNA encoding for firefly luciferase, the gene that causes fireflies to glow, to cancerous liver cells in an animal model, as a proxy for using SiLNPs to treat liver cancer. Wherever cells started to glow, the researchers could be confident that SiLNPs had transferred their mRNA payload to cells.

When glowing cells also appeared in the animal models' lungs, the researchers realized that certain SiLNPs variants were guiding the molecules outside the liver -- the holy grail of LNP research, since LNPs tend to congregate in the liver, due to that organ's convoluted network of blood vessels.

Among the changes the group identified that adjusted the trajectory of the SiLNPs were adjustments as small as substituting one chemical group for another -- an amide for an ester, in this case -- which led to a 90% success rate in delivering mRNA to lung tissue in the animal model.

"We just changed the structure of the lipids," says Xue, "but this small change in the lipid chemistry substantially increased extrahepatic delivery."

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The group also determined that a wide variety of chemical factors affected the SiLNPs' overall efficacy, including the number of silicon groups in the lipids, the length of the lipids' tails and the structure of the lipids themselves.

In addition, the SiLNPs had a marked affinity for endothelial cells; since blood vessels are made of endothelial cells, SiLNPs may have clinical applications in regenerative medicine that targets damaged blood vessels, in particular in the lungs. Indeed, the researchers found that SiLNPs delivering substances that promote new blood vessel growth dramatically improved blood oxygen levels and lung function in animal models suffering from a viral infection that damaged their lungs' blood vessels.

The researchers theorized that one reason for SiLNPs' effectiveness could be that silicon atoms are larger than carbon atoms. Because the atoms are less tightly packed, when SiLNPs fuse with target cell membranes, the former likely increases the fluidity of the latter. That extra flexibility in turn helps the mRNA carried by SiLNPs enter the target cell, so the mRNA can be used to produce proteins more readily. As the SiLNPs travel through the bloodstream, proteins that attach to their surface also help guide them to the right tissue.

Ultimately, the SiLNPs showed up to a sixfold improvement in delivering mRNA compared to the current gold-standard LNP varieties, suggesting that the unique properties of the siloxane composites have a pronounced effect on the molecules' clinical potential. "These SiLNPs show promise for protein replacement therapies, regenerative medicine and CRISPR-Cas-based gene editing," says Xue.

"We hope that this paper can lead to new clinical applications for lipid nanoparticles by showing how simple alterations to their chemical structure can enable highly specific mRNA delivery to the organ of interest," adds Mitchell.

This study was conducted at the University of Pennsylvania's School of Engineering and Applied Science (Penn Engineering), School of Veterinary Medicine (PennVet), Perelman School of Medicine (Penn Medicine); the University of Electronic Science and Technology of China; the University of Delaware; and Temple University and was supported by a U.S. National Institutes of Health (NIH) Director's New Innovator Award (DP2 TR002776), a Burroughs Wellcome Fund Career Award at the Scientific Interface (CASI), a U.S. National Science Foundation CAREER Award (CBET-2145491), an American Cancer Society Research Scholar Grant (RSG-22-122-01-ET), and the National Institutes of Health (NICHD R01 HD115877).



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Additional co-authors include Ningqiang Gong (co-first author), Xuexiang Han, Sarah J. Shepherd, Rohan Palanki, Junchao Xu, Kelsey L. Swingle, Rakan El-Mayta, Il-Chul Yoon and Jingchen Xu of Penn Engineering; Gan Zhao (co-first author), Zebin Xiao and Andrew E. Vaughan, of PennVet; Vivek Chowdhary, Mohamad-Gabriel Alameh, Claude Warzecha, Lili Wang, James M. Wilson and Drew Weissman of Penn Medicine; Xinhong Xong and Jiayi Cui of the University of Electronic Science and Technology of China; Darrin J. Pochan of the University of Delaware; and Karin Wang of Temple University.

Science Daily, 1 October 2024

<https://sciencedaily.com>

### Chloride ions tunnel free from PVC

2024-09-26

Quantum tunnelling is the dominant process driving chloride ions to leach from polyvinyl chloride (PVC), a computational study concludes.

Gbolagade Olajide and Tibor Szilvási of the University of Alabama, US, made the surprising discovery while studying a base-assisted E2 reaction in which a chloride ion is liberated from a PVC polymer chain. 'We did some exploratory calculations, then my student [Olajide] came back to me that, okay, this is the barrier, this is the energetics, and I see that the barrier is extremely narrow,' says Szilvási.

This was the first hint of a phenomenon called quantum tunnelling. In contrast to thermal activation, where reactants gain sufficient energy to jump the energy barrier of a reaction, the wave-like nature of electrons and nuclei means they can also seep through the barrier without possessing the requisite energy. But since the barrier weakens the wavefunctions exponentially, it must be narrow for tunnelling to be a realistic prospect.

Although he saw this slender barrier, Szilvási was still sceptical. 'I was just immediately thinking that this should not be the case. If you have chlorine, which is a really heavy atom, involved in a reaction, then normally there is no tunnelling at all.'

But further probing only strengthened the case. 'Everything still pointed to the same direction,' says Szilvási. 'Then we decided that we will do a really detailed study on this ... and that also showed the same answer.'

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The researchers used density functional theory (DFT), a widely used technique in computational chemistry, with less common add-ons to model tunnelling. By switching the tunnelling contributions on and off, they were able to compare the reaction rate that arose from tunnelling to that from thermal activation alone. They were astonished to find that in 93% of reactions at room temperature, the reactants burrowed through the barrier rather than jumping it.

Further calculations, in which they replaced various atoms by isotopes of different mass, pinpointed that hydrogen was leading the charge in this quantum escape. This might be expected, being the lightest element, but Szilvási makes the intriguing suggestion that 'somehow it drags the chlorine with it'.

Peter Schreiner, an organic chemist at Justus Liebig University Giessen, Germany, is similarly struck by the results. 'I was surprised that something as common and mundane as PVC would be affected by tunnelling,' he says, adding that it is the first time the effect has been demonstrated for a polymer.

Including quantum tunnelling in DFT calculations is costly in computer time, and thus tempting to dismiss as an exotic folly. Schreiner, who has long argued that tunnelling's importance is overlooked, is thrilled that the researchers have found such a stark example in an everyday reaction.

'I would say [quantum tunnelling is] alien to most people, and they think, oh it's probably not relevant to me,' he says. 'These authors have opened the gate for some real-time application – that is, how to get rid of certain plastics.'

PVC is the world's third-most produced plastic, used in everything from vinyl records and window frames to rainwear and inflatables. It is also a common choice for modern water pipes, and many old lead pipes are being replaced by PVC. Szilvási and Schreiner both highlight the issue of chloride leaching from underground pipes into the environment, particularly if buried in alkaline soil. Conversely, if PVC is to be recycled, the efficient removal of chloride and other additives is essential.

Szilvási cautions that while his work may explain chloride leaching, it doesn't offer a magic bullet to prevent it. 'Quantum tunnelling will always be there, and you cannot avoid it.'

Chemistry World, 26 September 2024

<https://chemistryworld.com>



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**PFAS Are More Toxic Combined**

2024-10-02

A new study has measured the toxicity of several types of PFAS when mixed together.

A first-of-its-kind study has measured the toxicity of several types of per- and polyfluoroalkyl substances (PFAS), better known as “forever chemicals,” when mixed together in the environment and in the human body.

The good news: Most of the tested chemicals’ individual cytotoxicity and neurotoxicity levels were relatively low.

The bad news: The chemicals acted together to make the entire mixture toxic.

“Though they are structurally similar, not all forever chemicals are made equal — some are more potent, others less. When mixed, all components contributed to the mixture’s cytotoxicity and neurotoxicity,” says the study’s first-author, Karla Ríos-Bonilla, a chemistry PhD student at the University at Buffalo.

“In the laboratory assays we used in this study, most of the types of PFAS that we tested did not appear to be very toxic when measured individually. However, when you measure an entire sample with multiple PFAS, you see the toxicity,” adds study co-author Diana Aga, PhD, director of the RENEW Institute, SUNY Distinguished Professor and Henry M. Woodburn Chair in the UB Department of Chemistry.

This research was conducted in collaboration with Beate Escher of the Helmholtz Centre for Environmental Research (UFZ), Leipzig, Germany, where Ríos-Bonilla did the in vitro toxicity experiments in the high-throughput screening facility CITEPro. It was published Sept. 11 in *Environmental Science and Technology*, a journal of the American Chemical Society.

The study is novel in that it assesses mixture toxicity of PFAS. These synthetic compounds have been widely used in consumer products — from nonstick pans to makeup — for decades, and they can take hundreds to thousands of years to break down, if ever. They are estimated to be in at least 45% of the nation’s drinking water and in the blood of practically every American, and they have been linked to cancer and neurodevelopmental disorders.

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Earlier this year, U.S. Environmental Protection Agency (EPA) issued the first-ever drinking water standards for six kinds of PFAS. However, it is estimated that there are over 15,000 varieties present in the environment. Only a handful of these chemicals have standards and are regulated.

“There are six PFAS that can be regulated because we know a lot about them and their toxicity. Unfortunately, we cannot regulate other forms of PFAS until their toxicities are known,” says Aga, who is principal investigator of the EPA STAR grant that funded the research. “We need to set maximum contamination levels for each PFAS that is proportional to their toxicity. To regulate contaminants, it is crucial to know their relative potencies when they occur as mixtures in the environment along with their predicted environmental concentrations.”

Other co-authors from UB are G. Ekin Atilla-Gokcumen, PhD, Dr. Marjorie E. Winkler Distinguished Professor and associate chair in the Department of Chemistry, and Judith Cristobal, PhD, senior research scientist.

Ríos-Bonilla is also supported by a graduate fellowship from the National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health (NIH).

**PFOA and PFOS are major contributors to mixture toxicity**

To conduct the study, researchers created their own PFAS mixtures, one that is representative of an average American’s blood serum, and the other of surface water samples found in the U.S. Ríos-Bonilla used data from the U.S. Centers for Disease Control and Prevention and from the U.S. Geological Survey to determine the average concentration ratios of PFAS in human blood and in surface water, respectively.

They then tested these mixtures’ effects on two cell lines; one that tests for mitochondrial toxicity and oxidative stress and the other for neurotoxicity.

Of the 12 PFAS spiked in the water mixture, perfluorooctanoic acid (PFOA) — commonly used in nonstick pans and firefighting foam — was the most cytotoxic, making up to 42% of the mixture’s cytotoxicity.

On the other hand, both PFOA and perfluorooctane sulfonic acid (PFOS) contributed roughly the same cytotoxicity (25%) to the neurotoxicity assay, despite both contributing only 10 and 15% to the mixture in terms of concentration, respectively.

The blood mixture had four PFAS present, but PFOA again was the most cytotoxic to both cell lines. Despite its molar contribution being only 29%,



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PFOA triggered 68% of the cytotoxicity in the cytotoxicity assay, and 38% in neurotoxicity assay.

Interestingly, when researchers analyzed the toxicity of the extracts from real biosolid samples collected from a municipal wastewater treatment plant, very high toxicities were observed despite the measured low concentrations of PFOA and other PFAS in the sample.

“This means that there are many more PFAS and other chemicals in the biosolids, which have not been identified, that contribute to the toxicity of the extracts observed,” Aga says.

### Synergistically versus additive

One of researchers’ goals was to determine if PFAS acts synergistically. This is when two or more chemicals’ combined effect is greater than the sum effect of the individual chemicals. However, their findings indicate that the effect of PFAS is concentration-additive: this means that an established mixture toxicity prediction model can be used to predict the combined effect of mixtures.

“As up to 12 PFAS in the mixtures acted concentration-additive for cytotoxicity and specific neurotoxicity, it is likely that the thousands of other PFAS that are in commerce and use are also acting in the same manner,” Escher says. “Mixtures pose more of a risk than individual PFAS. As they act and occur in mixtures, they ought to be regulated as mixtures.”

Researchers say the results of this study will also be very useful in assessing effectiveness of remediation efforts. Breaking down PFAS can sometimes create harmful byproducts that cannot be detected by chemical analysis, so measuring the toxicity of a sample after treatment may be the only way to judge whether a remediation technology is effective.

“Toxicity assays can be a complimentary tool when analytical chemistry doesn’t give you all the answers, especially when the identities of contaminants in the mixture are unknown, which is the case in many polluted sites,” Aga says.

Technology Networks, 2 October 2024

<https://technologynetworks.com>

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### Banned pigments found in tattoo inks sold in the EU

2024-09-26

Several common tattoo inks sold and used in Europe contain pigments banned under the region’s chemicals regulatory framework, according to new analysis out of John Swierk’s research group at Binghamton University in the US. His team is urging the industry to develop improved and standardised manufacturing protocols.

Specifically, the chemists investigated five green and five blue tattoo inks from five separate manufacturers that are distributed in Europe and marketed as being Reach (registration, evaluation, authorisation and restriction of chemicals) compliant. Reach not only forbids certain pigments but also mandates that all tattoo ink labels provide an accurate ingredient list with relevant hazard warnings.

Only one of the 10 inks analysed by the Binghamton group was Reach compliant. Nine contained material not listed on their labels.

Tattoo inks available in Europe are subject to stricter regulations than those in the US and other countries. In 2022, certain hazardous substances in tattoo inks, including the pigments Blue 15:3 and Green 7, were effectively banned under Reach over concerns that they cause cancer or genetic mutations. Four of the inks that Swierk’s team analysed contained Green 7, and they found Blue 15 in two of them but were unable to determine the particular polymorph of that pigment.

Regarding the EU restriction on the use of Blue 15:3 in tattoo ink, the chemists are now arguing that published methods using Raman spectroscopy are unable to distinguish between different Blue 15 polymorphs, highlighting a major challenge for Reach compliance. The Binghamton researchers underscore the need for a standardised protocol to differentiate between them in a manufacturing setting. They also raise the broader question of why only Blue 15:3 was banned under Reach while other polymorphs of that pigment were not.

The researchers also uncovered ingredients in some of the inks that are cause for concern, although not explicitly banned by Reach. These include polyethylene glycol and propylene glycol. Meanwhile, butylene glycol – thought to be a safer alternative to propylene glycol – was listed on a label of one of the inks but was not detected in any of them. In addition, one carrier solution contained isopropyl alcohol at an apparent concentration that is forbidden under Reach.



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Swierk's team's previous study in this area, published earlier this year, examined tattoo inks from nine US manufacturers and discovered that for more than 80% of them there were major discrepancies between their ingredients and their labels.

Chemistry World, 26 September 2024

<https://chemistryworld.com>

### Sustainably produced covalent organic frameworks can be used for efficient CO<sub>2</sub> capture

2024-10-01

An international research team headed by Heinrich Heine University Düsseldorf (HHU) and the University of Siegen has synthesized a new compound, which forms a so-called covalent organic framework. The compound, which is based on condensed phosphonic acids, is stable and can, for example, be used to capture carbon dioxide (CO<sub>2</sub>), as the researchers describe in Nature Communications.

Covalent organic frameworks (COFs) are a class of porous crystalline materials which form scaffold-like structures. The term "covalent" denotes that chemical bonds between the individual building blocks of the framework are formed via shared electron pairs.

A research team headed by Dr. Gündoğ Yücesan, Heisenberg Junior Research Group Leader at the Section for Nanoporous and Nanoscale Materials at HHU and Professor Dr. Jörn Schmedt auf der Günne, leader of the Inorganic Materials Chemistry group at the University of Siegen, now presents a simple approach to this family of frameworks, the members of which are particularly stable and promise great application potential.

Researchers from Berlin, Bremen, Saarbrücken, Turkey and the United Kingdom were also involved in the study.

The class of polyphosphonate covalent organic frameworks is characterized by phosphorus-oxygen-phosphorus bonds, which comprise simple organic phosphonic acid building blocks and—almost like Lego bricks—can be joined together by heating them to temperatures of just approx. 200 degrees Celsius.

Dr. Yücesan said, "The special property of these COFs is that, despite the mild synthesis conditions, they exhibit good water and water vapor stability, meaning that—by contrast with compounds developed to date—they can be used in water and electrolytes."

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A further milestone was the development of a sustainable synthesis route. Yücesan said, "For the first time, a solid-state synthesis process has been developed for COFs, which can be realized completely without solvents. This method enables low-cost, scalable production from kilograms to tons, making it more cost-effective compared with other microporous materials.

One challenge for the researchers was that the compounds did not crystallize well and are amorphous. They succeeded in finding evidence for the bonds by means of nuclear magnetic resonance.

Professor Schmedt auf der Günne said, "If we had not been able to use the common states of neighboring phosphorus atom nuclei, the bonding structure of the substance would have remained in the dark and the properties would not have been understood."

Polyphosphonates of this type have great application potential. The framework structures can capture the harmful greenhouse gas CO<sub>2</sub>. A slight change in pressure can release it again.

"Such substances are needed for waste gas cleaning and to prevent greenhouse gas emissions," the authors of the study noted.

Phys Org, 1 October 2024

<https://phys.org>

### Scientists develop novel method for strengthening PVC products

2024-10-03

Researchers have developed a way to make one type of plastic material more durable and less likely to shed dangerous microplastics. Their study has identified a secure way to attach chemical additives to polyvinyl chloride (PVC). The work is published in the journal Chem.

Found in everything from toys, construction supplies and medical packaging, PVC plastics currently rank third among the most used plastics worldwide. Despite its widespread use, pure PVC is brittle and sensitive to heat, and manufacturers can only utilize it after stabilizing its properties with other chemicals.

However, these additives, or plasticizers, are only a short-term fix for stabilizing PVC. Over time, plasticizers leach from the plastics, which allows the material to deteriorate into potentially hazardous organics and microplastics. Now, a team led by Christo Sevov, the principal investigator



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of the study and an associate professor in chemistry and biochemistry at The Ohio State University, has found that using electricity to permanently affix those chemical additives can prevent such unwanted reactions.

“Instead of mixing in those chemicals, our method involves chemically bonding the plasticizer compound directly to PVC by grafting them onto the backbone of the polymer,” said Sevov.

Altering PVC molecules in this way allows for them to become more durable and resistant to chemical changes, eventually leading to materials with more robust properties.

“This is really one of the few examples that we have where there’s this much control over changing the properties of PVC,” said Sevov. “So this is the first step in controllably modifying PVC to give it properties you’re interested in, whether it’s hard, stretchy or soft.”

The team did run into some challenges; synthetic polymer modifications often fail because the reactions were originally developed for small-molecule analogs, not big-molecule analogs such as pure PVC. To solve this, researchers optimized the catalyst they used in their process, and through trial and error, were able to overcome the issues that arise when editing big molecules.

Outside of making leaps in organic chemistry, the team’s work also has implications for the environment, as putting a cap on how quickly plastics degrade can do much to curb the release of microplastics—tiny pieces of plastic debris—into our surroundings.

Today, scientists know that these particles, which have been found to pollute the air, water and our food supply, are harmful both to humans and wildlife. The average person likely ingests between 78,000 and 211,000 of these particles every year.

But as experts are beginning to understand the long-term impact microplastics have on Earth, organic chemists are racing to find ways to phase them out of everyday life, said Sevov.

“Many chemists are shifting their efforts to studying big molecules and developing new chemistries for upcycling, recycling and modifying well-known polymers,” he said. For example, trying to recycle PVC products can cause further degradation to the material due to the high temperatures it takes to convert plastic into something else, so the process isn’t very efficient.

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But using Sevov’s method, “You can potentially reuse the material many, many more times before it really begins to fall apart, improving its lifetime and reusability,” he said.

In the future, more control over which materials will be safe for consumers will come once efforts to fix PVC leakage can be reliably scaled up, something that the study emphasizes that, at the moment, is possible with their method alone.

“There’s no better way to do this on the scale you would need for commercial PVC modification because it is an immense process,” said Sevov. “There’s still a lot to play around with before we solve the microplastic situation, though now we’ve laid the groundwork for how to do it.”

Other Ohio State co-authors include Jordan L.S. Zackasee, Valmuri Srivardhan, Blaise L. Truesdell and Elizabeth J. Vrana.

Phys Org, 3 October 2024

<https://phys.org>



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### Chemicals used in many popular food and drink products now banned from California public schools

2024-10-01

California Governor Gavin Newsom has signed into law a bill that bans the use of red dye No. 40 and five other chemicals from use in foods served at public schools.

On Saturday, September 28, the Golden State became the first in the country to pass a law forbidding the use of the ingredients found in some popular cereals, ice creams, drinks, candy, ice pops, cheese-flavored chips, jellies and more, according to the Environmental Working Group, a nonprofit environmental health organization that cosponsored the law with Consumer Reports. The law will be enacted on December 31, 2027.

Known as the California School Food Safety Act and introduced by Democratic Assemblymember Jesse Gabriel in February, Assembly Bill 2316 prohibits a school district, county superintendent of schools or charter school with grades kindergarten through 12th from offering foods or beverages containing red dye No. 40, yellow dyes Nos. 5 and 6, blue dyes Nos. 1 and 2, and green dye No. 3. Some of these dyes are found in some, but not all, products under the Cheetos, Doritos, Skittles, M&Ms, Starburst, Gatorade, Mountain Dew, Cap'n Crunch, Ruffles and Takis brands.

CNN has reached out to the owners of these brands for comment. Barcel USA, manufacturer of Takis, declined to comment.

California is home to the largest public school system in the nation, with more than 6.3 million students and 10,000 schools, Tony Thurmond, state superintendent of public instruction and bill cosponsor, said in a news briefing hosted by the EWG on August 6.

The bill stems from concerns these dyes would harm children's ability to learn, as they have been linked to behavioral difficulties and decreased attention among children, according to a 2021 study by the California Office of Environmental Health Hazard Assessment.

"California is once again leading the nation when it comes to protecting our kids from dangerous chemicals," Gabriel said in a news release.

The law is "important to me as a parent, it's important to me as somebody who's struggled with ADHD as a child, and it's important to me as a parent of a child who is struggling with ADHD," Gabriel said in the August briefing. "We know that the synthetic food dyes that are targeted by this bill can

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cause harm for all kids, but we know that there is a specially pronounced impact on a lot of our young people with ADHD and other challenges."

Gabriel and the EWG said that though "new science is available," the US Food and Drug Administration's current regulations of the dyes in food is based on research that's 35 to 70 years old.

CNN has reached out to the FDA for comment.

"Reassessing the safety of chemicals in food as new, relevant data become available is a priority for the FDA," the agency said in a statement in August, when the bill was passed by the California Legislature. "The FDA has reviewed the research on the effects of color additives on children's behavior including the literature review cited by the Bill. The totality of scientific evidence shows that most children have no adverse effects when consuming foods containing color additives, but some evidence suggests that certain children may be sensitive to them."

In addition to the FDA's own evaluations, the agency also supports and participates in international risk assessments conducted under the Joint Food and Agriculture Organization of the United Nations/World Health Organization Expert Committee on Food Additives.

"All the colors listed have recently undergone assessments for safety in food by the JEFCA and were found to be safe for use in food under current use conditions," the FDA said.

However, the agency will continue to assess the emerging science and ensure the safety of approved color additives, including a public meeting it hosted in September to review the process for post-market assessment of chemicals in food, according to the statement.

### Impacts of AB 2316

John Hewitt of the Consumer Brands Association, which represents more than 1,700 brands, said in a statement in August that "it's unfortunate that scientifically proven, safe ingredients have been demonized for the purpose of advancing a political agenda.

"No industry is more committed to food safety than the consumer packaged goods industry. It's why we have urged the FDA to aggressively acknowledge its responsibility as the nation's food safety regulator," Hewitt, senior vice president of packaging and sustainability and state affairs at the association, said via email. "The passage of this bill could cost



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schools and families money, limit choice and access, and create consumer confusion.”

But Thurmond stressed the greater importance of “the cost of our failure to act ... in a nation where our children already have some of the highest rates of illness, asthma, diabetes (and) heart disease,” compared with other countries.

Gabriel echoed these sentiments, adding that the bill may ultimately save California money by reducing the use of resources necessary for helping children struggling in the classroom.

“I see this both through personal experience and also the work that I do as a lawmaker,” he added. “It’s really expensive.”

Newsom’s decision renders the United States food environment more in alignment with that of the European Union, where products including these dyes are required to have a warning label saying those products could harm young people, Gabriel added.

“The point of this bill is to encourage manufacturers to make minor modifications to their recipes, so that they can serve the same foods that we all love, that our kids love, but without these dangerous chemicals that harm people,” he added. “We have incredible confidence that they’re able to do that ... because they make the same products in so many countries around the world, just without the harmful chemicals.”

The EWG has noted in the past that few foods available in California schools use the ingredients the bill bans.

However, Gabriel and other assemblymembers believe that given the size of California’s economy, the law is a “major victory for the food safety movement not only here in the state of California, but also nationally,” he said, also noting that more than 70 organizations support the bill.

After the state banned brominated vegetable oil, used mostly in some sodas, as part of its California Food Safety Act in October 2023, the US Food and Drug Administration revoked the regulation for its use nine months later.

And at least 10 other states have begun following California’s lead, introducing legislation based on the act, Gabriel said.

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### Avoiding these chemicals in food

If you’re concerned about the potential impacts of these dyes on your child’s health, you can help them avoid them by checking the ingredient lists of any products you buy, experts said — particularly packaged foods, which are typically ultra-processed and thus are more likely to include artificial dyes, according to the EWG.

You can also try alternatives without those ingredients — foods that are USDA-certified organic, for example, can’t contain artificial food dye. Cut back on sodas, juices or sports drinks that might contain them, as well. Offering kids substitutes may be more effective than flat-out denial of something they’re craving.

“Emphasize brightly colored produce,” the EWG suggests. “The best competition for splashy packages of ultra-processed foods is the rainbow of colors in fresh fruit and vegetables.”

Actress Lesley-Ann Brandt has ongoing conversations with her 7-year-old son about which foods are more or less healthy to eat and why, she said in the briefing.

“We talk to him as if he’s an adult, and he knows we don’t eat this because of this, but here’s an alternative,” Brandt said. “We make some of our foods too, and it’s a way to discuss nutrition.”

Brandt has witnessed the benefits of nutrition in her family of origin, too, she added. After growing up in two “very different” food systems of South Africa and New Zealand, “I really noticed the difference coming to the States 14 years ago,” she said.

“I’m also the oldest sister of a brother who had severe ADHD as a child, so I got to see firsthand the impact of nutrition and how it helped him,” Brandt said. “One of the first things my mother did to try and avoid heavily medicating him was to look at his nutrition and the processed sugars, ingredients, food dyes and synthetic chemicals that just (were) not going to serve him in school.

“And it was really the difference between a B student and a C student for him,” she said. “That impacted his confidence as well.”

CNN, 1 October 2024

<https://edition.cnn.com>



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### Developing novel chiral capsule tools for advanced optical technologies

2024-10-02

Chirality is an essential property in biology; the molecular building blocks of some of the most important biological structures, including DNA and proteins, are chiral. When a molecule is said to be chiral, it means that it is distinguishable from its mirror image, much like how one's left hand cannot be superposed onto the right hand. Interestingly, chirality can also affect how a molecule or a molecular aggregate emits or responds to light, especially circularly polarized light.

With the rise of advanced optical technologies, such as chiroptically active components could find applications in modern displays, optical storage systems, analytical tools, and biomedicine. Thus, scientists have been exploring innovative ways of making well-established non-chiral dyes behave like chiroptically active molecules.

Through a process known as chirality transfer, dyes encapsulated in cavities made from chiral molecules can acquire chiroptical properties. However, the synthesis of usable chiral capsules has proven challenging, with existing designs being complex and inflexible.

In a recent study published in the *Journal of the American Chemical Society*, a research team including Assistant Professor Yuya Tanaka and Yoshihisa Hashimoto from Institute of Science Tokyo has developed a new, simpler solution. They created novel chiral capsules based on terpenes, a class of natural compounds from plants. The terpene-based capsules offer an efficient and flexible way to transfer chirality to various non-chiral dyes in the cavity.

The present chiral capsules are composed of terpene-based bent amphiphilic molecules, obtained through a series of chemical modifications on menthol. The chiral amphiphiles, due to their hydrophilic and hydrophobic frameworks, spontaneously form globular structures called terpene capsules when mixed with water. When a non-chiral dye is mixed with the amphiphiles, a host-guest composite structure is formed, in which the dyes are accommodated in the chiral cavity.

Through extensive experiments, the researchers showed that chirality transfer occurred between the capsule and several types of non-chiral dyes. For example, fluorescent dyes, including polyaromatic and BODIPY compounds, exhibited strongly induced circular dichroism and circularly polarized fluorescence.

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Unlike previously reported chiral hosts, the present structure was highly versatile and easy to produce, as Dr. Tanaka remarks, "Our terpene capsules facilitate the easy preparation of well-defined host-guest composites with tunable chiroptical properties through simple uptake of various non-chiral dyes, unlike the majority of previously reported hosts with rigid chiral cavities."

Another notable advantage of this chiral capsule is that the resulting composites can be used in water without the need for organic solvents, which was a limitation of other designs.

Overall, this study has the potential to lead to affordable, high-performance chiroptically active composites, which in turn would pave the way to advances in cutting-edge optical technologies. "Our strategy allows for the straightforward introduction of chirality to various non-chiral dyes without elaborate synthetic modification, highlighting its potential application to polymer materials and catalysts," concludes Dr. Tanaka.

"Based on the present findings, an ongoing research project in our laboratory focuses on multicomponent host-guest systems with higher chiroptical functions," he adds, hinting at future developments.

Phys Org, 2 October 2024

<https://phys.org>

### Weight Loss Drugs May Help To Fight Fatty Liver Disease

2024-09-19

A new finding into how the liver metabolizes fat indicates weight loss drugs could fight fatty liver disease.

In the fight against fatty liver disease, researchers are looking for any and all possible solutions.

But to combat the disease, which is also known as metabolic dysfunction-associated steatotic liver disease, or MASLD, scientists must first understand how the liver metabolizes fat. MASLD is on the rise in the U.S., now affecting nearly 40% of adults. The condition occurs when the body deposits extra fat in the liver, leading to inflammation, fibrosis and, in some cases, permanent liver damage or liver cancer.

A new study by researchers at Yale School of Medicine (YSM), published Aug. 27 in the journal *Cell Metabolism*, finds that people with MASLD burn fat in their livers at the same rate as people without the disease. The



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study, whose senior author is Gerald Shulman, MD, PhD, George R. Cowgill Professor of Medicine (Endocrinology) and professor of cellular and molecular physiology at YSM, appears to settle this question, which has been in dispute in the field.

The researchers also found that increasing blood levels of the glucose-related hormone glucagon stimulates liver metabolism in both healthy people and people with fatty liver disease. That's important because some experimental weight loss and diabetes drugs such as retatrutide also contain a glucagon agonist component—a welcome finding that suggests these drugs seem to be combatting fatty liver disease through multiple mechanisms.

Shulman points out that, while some medications exist to treat fatty liver disease, including the newly FDA-approved drug resmetirom, these treatments don't work for all patients.

"It's clear that we need other agents," he said, suggesting that therapies that rev up the liver's mitochondrial fat oxidation could be a useful approach.

### How to boost liver metabolism

Mitochondrial oxidation is the metabolic process liver cells use to convert fat to energy. If researchers could identify a way to increase liver mitochondria's fat-burning powers, that could reduce fat deposits in the liver and possibly even reverse MASLD and metabolic dysfunction-associated steatohepatitis (MASH). What was unclear, however, is whether these conditions on their own increase mitochondrial oxidation, since previous studies had differing conclusions. If fatty liver already raises the organ's fat metabolism, it seemed possible that trying to boost the metabolism even more would not have any effect against the disease.

Hoping to put that question to rest, Shulman and his team used a technique they recently developed known as positional isotopomer NMR tracer analysis, or PINTA. Many past studies had examined liver metabolism in cells or in test tubes in the lab, because it is very difficult to follow metabolic reactions as they happen in the body. But that natural context is critical and can change metabolism significantly as compared to artificial settings, Shulman said. In their method, study volunteers were infused with a mixture of three stable (non-radioactive) isotopes that allowed the scientists to trace the metabolism of the labeled substrates (surfaces acted upon by enzymes) and quantify rates of liver mitochondrial oxidation and gluconeogenesis as it happens in the body.

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Using this approach, they looked at liver fat metabolism in 12 healthy volunteers and compared it to that of 13 study volunteers with MASLD (fatty liver with inflammation) and 13 volunteers with the related condition metabolic dysfunction-associated steatotic liver, or MASL, a less severe form of fatty liver. They found that all three groups had the same rates of mitochondrial oxidation in the liver, which contrasted with the findings of some previous studies, affirming others. They also gave study volunteers infusions of glucagon, a hormone that stimulates glucose production. The hormone bumped up rates of hepatic mitochondrial fat oxidation in the healthy volunteer and MASL groups by 50 to 75%.

"This suggests that increasing glucagon will have additive beneficial effects to reduce liver fat, not only by reducing energy intake, but also increasing hepatic energy expenditure," Shulman said. People taking certain weight loss medications that also alleviate fatty liver have diminished appetites and generally consume fewer calories, reducing their overall energy intake.

The glucagon finding indicates that medications that boost levels of the hormone could treat fatty liver by increasing energy expenditure. It's known that GLP-1 agonist drugs such as semaglutide (Ozempic) can alleviate excess liver fat present in MASLD by promoting weight loss and reducing overall energy intake. Shulman and his colleagues are trying to find approaches that also increase fat metabolism. Indeed, experimental combination drugs that pair GLP-1 agonists with compounds that raise levels of glucagon have recently been found to effectively treat fatty liver disease.

Next, Shulman and his team want to use their method to test the effects of these and other metabolism-related drugs on liver metabolism. They also want to follow study volunteers with MASLD and MASH for a longer period to see whether the beneficial effects of glucagon on liver metabolism persist, which would be important for any successful treatment.

Technology Networks, 19 September 2024

<https://technolynetworks.com>

### Study coordinates satellite swarm for 3D imaging inside clouds

2024-09-30

David Stanley's interest in climate change led him to develop a program to improve how we gather data to study the inside of a cloud. The program



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simulated multiple satellites, collecting images of a cloud from many angles at the same time, which could help us to better understand what's happening inside the cloud.

"Normally, we can only see the outside features of a cloud," Stanley said. "Computed cloud tomography gets its name from computed tomography which is like a CT scan. Instead of X-rays, satellites take images of the cloud from as many angles and in as short a period of time as possible."

Stanley said one of the unknowns in climate modeling is how much convective transport affects regrowth of new clouds. Convection is about the movement of heat and moisture in the atmosphere, especially up- and down-drafts in unstable conditions.

"By generating multiple time passes on the center of the same cloud, you can see how the convection changes over time, how that is affecting the growth of other clouds in the future. And cloud growth can increase greenhouse effect."

Stanley said after completing his master's degree in aerospace engineering at the University of Illinois Urbana-Champaign, he reapplied to continue for a Ph.D. at Illinois.

"I talked about my general interest in engineering and space engineering, but also how important it is for us to better understand climate change and work toward finding solutions," he said. "Robyn Woollands saw that interest in me and asked me to join her research group. She connected me with Federico Rossi and Amir Rahmani in the Multi-Agent Autonomy Group at NASA's Jet Propulsion Laboratory and they introduced me to JPL scientists Changrak Choi and Anthony Davis who are knowledgeable about cloud tomography, atmospheric clouds and aerosols. It aligned with some of my interests, and it was something Robyn was looking at as an interesting mission proposal -- using multi-agent systems to support Earth science missions."

For the simulation, Stanley used a mixed integer linear program solver that is used for lots of different kinds of applications. Stanley wrote the code to develop a scheduler that would optimize the timing and camera pointing angles for the swarm of satellites to get as many images of the cloud as possible.

"What was interesting about this is how we used the mixed integer linear programmer to automatically determine the most efficient pointing pattern for the formation of the satellites. All the satellites had to point at

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the same target at the same time. But there could be dozens of different targets below each satellite, and there might be some targets that get missed if they're not pointed at the right time."

The goal was to maximize how many times the satellites saw different targets throughout the orbit.

"We ran two different simulations. We have one simulation of clouds generated on the surface of the Earth with a specific lifespan. In the computer, they're just a coordinate on a sphere. The second simulation propagates the satellite swarm. This can be done simply or using more complex, more accurate models.

"When we combine the data from those two simulations, the program calculates information about where the satellites are at different points in the orbit, and where the clouds are at the point in the orbit, then decides what the optimum looking pattern is between those satellites, and the clouds on the ground."

He said there were quite a few times in the midst of the study where he had different ideas about the best way to simulate the data and to pass on the data to the solver.

"Maybe you need just an array for every time step, and every satellite, or you could have an array for different sections of the Earth. I tried using different sections of the Earth as pointing coordinates at first by subdividing everything by brute force. But there's a lot of area on the Earth. And you end up with millions and millions and millions of indexes which on a desktop computer is not solvable."

In the end, Stanley said he drew on inspiration from Woollands' previous work. She had developed a method for a constellation of satellites orbiting Mars to collect as many observations of dust devils on Mars as possible, where, instead of subdividing the whole earth, they subdivided sections below the satellites which allowed them to only need a few indexes at a time.

"So, in addition to that, I was able to realize that I could actually use just the clouds themselves as the index," Stanley added. "It worked well and went down from millions of indexes to about a few 100 at a time, which is much more solvable."

Stanley stressed that this is simulated data.



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“We have made some assumptions about where the clouds are being created and where they’re going so there is a lot of room for this study to be improved and to look at more real-world data instead of generating our own. The important thing is that we have developed a new method that has the potential to significantly improve how 3D cloud data is collected which could lead an improvement in our understanding of the dynamics inside a cloud and hence long-term climate effects.

Science Daily, 30 September 2024

<https://sciencedaily.com>

### Seeing double: Designing drugs that target ‘twin’ cancer proteins

2024-10-01

Some proteins in the human body are easy to block with a drug; they have an obvious spot in their structure where a drug can fit, like a key in a lock. But other proteins are more difficult to target, with no clear drug-binding sites.

To design a drug that blocks a cancer-related protein, Scripps Research scientists have taken a hint from the protein’s paralog, or “twin.” Using innovative chemical biology methods, the scientists pinpointed a druggable site on the paralog, and then used that knowledge to characterize drugs that bound to a similar—but more difficult to detect—spot on its twin. Ultimately, they found drugs that only bound to the protein of interest and not its highly similar sibling.

Their approach, described in *Nature Chemical Biology* on September 18, 2024, and dubbed “paralog hopping,” could uncover new binding sites for drugs and inform drug development more broadly, since nearly half of the proteins in human cells—including many involved in cancer and autoimmune diseases—have such paralogs.

“This method may be generally useful in cases where you have paralogs, and you are trying to find a new drug for one of them,” says senior author Benjamin Cravatt, Ph.D., the Norton B. Gilula Chair in Biology and Chemistry at Scripps Research. “Being able to target one paralog over another is an important goal in drug development, as two paralogs often have different functions.”

Many genes have duplicated throughout evolution, resulting in multiple copies in the human genome. In some cases, copies have evolved slightly

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different sequences from each other, making their corresponding proteins into paralogs. These protein paralogs remain highly similar in structure and often have redundant or overlapping functions within cells.

In recent years, Cravatt’s research team formulated an approach to develop drugs that bind to the amino acid cysteine—a protein building block with unique, highly reactive chemical properties. The scientists’ method takes advantage of cysteines as an optimal site for drugs to attach to a protein permanently, often inactivating it. However, not all proteins have accessible cysteines. In the case of paralog pairs, one protein may have a druggable cysteine that the other does not.

“We started with this idea that if you know how to drug one protein, you can figure out how to drug its paralog in a similar way,” says Yuanjin Zhang, a graduate student at Scripps Research and first author of the new paper.

As a test case, the team tackled the paralog pair known as CCNE1 and CCNE2. Both proteins have been found to be overactive in breast, ovarian and lung cancer. However, scientists suspected that the two proteins play slightly different roles. The team posited that turning off just one protein could make treating some cancers more effective.

It has been difficult, however, to design drugs that target the CCNE1 and CCNE2 proteins to test this hypothesis. Cravatt, Zhang and their colleagues knew that CCNE2 had a druggable cysteine, while CCNE1 did not. If they could identify drugs that bound to the same spot on CCNE1, even in the absence of a cysteine, they suspected the protein would shut off.

The scientists first engineered a cysteine into CCNE1, mimicking the drug-binding spot they had pinpointed in CCNE2. They then leveraged this neo-cysteine to identify drugs that bind to CCNE1. Next, they screened a library of other chemical compounds for the ability to compete with that drug in binding to CCNE1. The team reasoned that some of the compounds that competed for the same spot would bind in ways that did not rely on the cysteine.

Indeed, Cravatt, Zhang and their colleagues discovered multiple compounds that could bind to the same site on CCNE1 even when the cysteine was removed again. Some compounds did not bind to CCNE2. Some also had opposite functions, stabilizing the molecule so that it might be more active than usual, rather than inactivating it. Structural studies revealed that the CCNE1 compounds bind to a cryptic pocket that was not previously known to be druggable.



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The team says the approach highlights the importance of screening for drugs in diverse, creative ways.

“If we had just screened looking for compounds with a particular function, we would not have identified all of these various functional molecules, and if we had just looked at the structure of CCNE1, we would not have found this binding pocket at all,” says Zhang.

More research is needed to discover whether the new compounds have potential utility in treating cancer or other diseases in which CCNE1 plays a role. Next, the scientists plan to apply their paralog-hopping method to other pairs of proteins important for tumorigenesis.

In addition to Cravatt and Zhang, authors of the study include Zhonglin Liu, Sang Joon Won, Divya Bezwada and Bruno Melillo of Scripps; and Marsha Hirschi, Oleg Brodsky, Eric Johnson, Asako Nagata, Matthew D. Petroski, Jaimeen D. Majmudar, Sherry Niessen, Todd VanArsdale, Adam M. Gilbert, Matthew M. Hayward, Al E. Stewart and Andrew R. Nager of Pfizer, Inc.

Phys Org, 1 October 2024

<https://phys.org>

### “Bioactive Glass” Bone Cancer Therapy Kills 99% of Osteosarcoma Cells

2024-09-18

In laboratory tests, the gallium-doped glasses killed 99% of osteosarcoma (bone cancer) cells while leaving non-cancerous cells largely unharmed.

Bioactive glass could one day be used as a novel treatment for bone cancer, new research suggests.

In laboratory cell culture tests, researchers found that samples of bioactive glass doped with gallium oxide were able to kill more than 99% of osteosarcoma cells without being cytotoxic to non-cancerous human osteoblasts. The research was published in Biomedical Materials.

#### What is bioactive glass?

Bioactive glasses are a type of biomaterial routinely used as a filler in dentistry and reconstructive surgery. The glasses are extremely biocompatible, ensuring they won't be rejected when implanted in the body, and provide a stable surface for bone and bodily tissues to

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bond with during the healing process. Additionally, the glasses are biodegradable and can even be formulated to release biologically active ions – such as calcium – that help to promote bone growth.

While there has been significant volumes of research looking into the use of these bioactive glasses for bone tissue engineering, comparatively little work has been done on using the materials for the targeted and controlled release of anti-cancer agents that could treat bone cancer.

“Bioactive glass is soluble glass that contains calcium and phosphorous, which are the key building blocks for bone. Bioactive glasses are normally to repair and regenerate bone and enamel,” senior study author Richard Martin, a professor in the College of Engineering and Physical Sciences at Aston University, told Technology Networks. “We wanted to make a material that could not only kill cancer cells but also help regenerate the bone void which is left behind after the surgeon removes the bone tumor.”

#### Beating bone cancer with bioactive glass

Osteosarcoma is the most common form of primary bone cancer, yet despite advances in chemotherapy and surgical interventions to remove tumors, osteosarcoma survival rates have only risen by 15 percentage points in the past 50 years. Bone cancer patients are also more susceptible to bone fractures and breaks, which can be an additional source of distress and pain.

For their experiments, the Aston University team formulated a novel bioactive glass doped with gallium oxide in different concentrations. These were then ground down into small particles and sieved before use.

“We are using gallium, which is chemically very similar to iron,” Martin said. “Cancers tend to grow much more rapidly and therefore uptake any nutrients/or ions present. So they naturally absorb the toxic gallium.”

Glasses containing 5 mol% gallium oxide were found to reduce the viability of osteosarcoma cells by 99% with no significant reduction seen in healthy control cells, even after 10 days of exposure.

Energy-dispersive X-ray spectroscopy tests also indicated the formation of an amorphous calcium phosphate/hydroxyapatite layer on the surface of the bioactive glass particles following seven days of exposure to simulated body fluids, indicating the beginnings of new bone growth. This additional bone growth is significant as it indicates the potential of these glasses to stimulate bone regeneration after treatment.



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“Bone cancer patients tend to have a lower bone density and be more susceptible to fractures. The gallium-doped bioactive glasses will help regenerate bone strengthen the area and hopefully prevent fractures,” Martin said.

In previous studies with 3 mol% gallium oxide bioactive glass, the research team had been able to kill around 40% of osteosarcoma cells, a figure deemed too low to form the basis of future treatments. With these new tests, Martin believes that bioactive glasses of this type could one day lead to effective, localized treatments for bone cancer that also help to regenerate diseased bones.

The team is now hoping to conduct further research with partners and begin trials using gallium-doped bioactive glasses.

“We will be working together with the Royal Orthopaedic Hospital to isolate patient-derived cancer cells and test out the materials against these cells,” Martin said.

Technology Networks, 18 September 2024

<https://technologynetworks.com>

### Beyond hydrogen bonding: new definitions for secondary bonding interactions to end confusion

2024-10-01

Proposals for the new definition of the tetrel bond will be available for community review in 2025, according to the International Union of Pure and Applied Chemistry's (IUPAC) committee chair Giuseppe Resnati. The announcement follows the release of the pnictogen bond recommendations earlier this year as part of a 20-year mission to formally clarify the terminology around secondary bonding interactions after decades of confusion and misuse.

As a fundamentally non-visual discipline, chemistry needs clear and well-defined nomenclature to provide a reliable and meaningful way for researchers to convey their findings to others. While the hydrogen bond is universally recognised by the chemistry community, its more obscure relatives – the halogen, pnictogen, chalcogen and tetrel bonds – are often overlooked, either misnamed or misclassified as other types of interaction. In recent decades, this widespread misuse of terminology created a disjointed and inconsistent base of knowledge within the literature which, in 2004, IUPAC decided to tackle head-on.

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As the professional organisation responsible for standardisation in chemistry, IUPAC brings together researchers from across the chemical sciences to create a universal scientific language. All recommendations hold a legal status, with feedback and consensus from the wider community playing a vital role in every new project. But as chemistry evolves, so must its terminology, meaning a huge part of the organisation's role is to challenge existing definitions and conventions which no longer reflect a modern understanding of chemistry.

### Naming problems

Secondary bonding interactions are a prime example of this very issue. These weak, non-covalent interactions underpin research areas as diverse as catalysis, supramolecular chemistry and biological chemistry, with hydrogen bonds the most widely recognised example.

For over 60 years, it was believed that hydrogen was the only element capable of forming these bonds and the terms 'secondary bonding interaction', 'non-covalent bond' and 'hydrogen bond' were often used relatively interchangeably. Research in the 70s later identified halogen atoms participating in similar interactions and subsequent studies demonstrated that other p-block elements could also form analogous bonds.

This greater nuance, coupled with the lack of specific names and definitions for these newly discovered interactions created a degree of confusion in the field. 'People were using this terminology wrongly in the literature or proposing new names and definitions. Different communities were using different terms to say exactly the same thing,' says Pierangelo Metrangolo, a supramolecular chemist and IUPAC officer. 'We realised there was a need to distinguish each of these interactions clearly.'

Metrangolo, as part of an IUPAC committee, has spent the last 20 years working on projects to develop a series of definitions and supporting documentation to help researchers more effectively identify and classify these secondary bonding interactions. Each recommendation includes an explanation of the key features of the bond, followed by a list of characteristic experimental and theoretical evidence for the interaction.

'People need to have authoritative documents they can refer to where there's a clear definition, but also a long list of notes where you can get the parameters. If many of the conditions are met, you know you've encountered that kind of interaction,' says Metrangolo.



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Earlier this year, the team released a definition for the pnictogen bond – the group 15 analogue of the hydrogen bond – with a final recommendation for group 14's tetrel bond expected in several years' time. Crucially, this definition, as with others in the series, emphasises the fundamental nature of the interaction. The named donor atom (the pnictogen) acts as the electrophile, creating a predominantly electrostatic attraction towards a nucleophilic region of the acceptor. 'The aim was to stress that, due to an anisotropic distribution of the electron density resulting from the covalent bonds formed by the pnictogen atom to other atoms in the molecule, some of the outer surface can be electrophilic, even for elements commonly perceived as Lewis bases,' explains Resnati.

By explicitly naming interactions according to the electrophilic contributor, the new terms enable a clear distinction between similar bonds, which in turn gives researchers a vital tool to influence those interactions. 'If we can distinguish between a hydrogen bond and a pnictogen bond, we can think about the factors contributing to the force there,' explains Steve Scheiner, another committee member, specialising in computational chemistry. 'But many people don't easily accept the idea that two electronegative atoms can actually form an attractive interaction.'

This lack of awareness is an ongoing issue, with many researchers misclassifying their intermolecular interactions as more familiar hydrogen bonds. However, it was the team's original work on redefining the hydrogen bond back in 2011 that first revealed the extent of this problem and began to take the first steps to address this systemic miscommunication.

#### Evolved understanding

The hydrogen bond was first identified over 100 years ago and was originally defined as 'a weak electrostatic chemical bond which forms between covalently-bonded hydrogen atoms and a strongly electronegative atom with a lone pair of electrons' – which in practice meant nitrogen, oxygen or fluorine.

However, over the second half of the 20th century, a growing body of evidence suggested that perhaps this narrow definition didn't tell the whole story. 'It was considered early on that a CH group was incapable of forming a hydrogen bond. But in the 50s, some crystal structures were published which looked like they had CH–O hydrogen bonds,' says Scheiner. 'This was quickly poo-pooed by other crystallographers who argued no matter what it looked like, it couldn't be a hydrogen bond because it was a CH.'

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The spectroscopic criteria for identifying a hydrogen bond were also called into question. An early characteristic sign was red shifting in the IR spectrum – the covalent bond involving the shared hydrogen produced a broader peak shifted towards a lower frequency. However, by 1998, conclusive cases began to emerge where this bond's frequency was actually shifted in the other direction (known as a blue shift), triggering further disagreement as to whether these interactions could be called a hydrogen bond.

In 2004, IUPAC formed a committee to evaluate and refine the existing definition of the hydrogen bond to reflect this contemporary understanding and the team were careful to avoid the limitations of the former definition. 'When you have to describe a phenomenon you can focus on many key features – the nature of the interaction, the geometric features etc – but what characterises all these approaches is that you make an emphasis of one feature over the others,' says Resnati who joined the team in 2010. 'The decision made when we started this was not to focus on the understanding of the interaction which may evolve with time, not on any one feature of the interaction, but on the very essence.'

After seven years, having evaluated an immense body of literature documenting this evolving understanding of the hydrogen bond, the team proposed a new definition alongside a list of criteria and characteristics to support researchers in confidently identifying this type of bond.

'The hydrogen bond is an attractive interaction between a hydrogen atom from a molecule or a molecular fragment X–H in which X is more electronegative than H, and an atom or a group of atoms in the same or a different molecule, in which there is evidence of bond formation.'

But, despite the extensive supporting explanation, the new definition initially proved controversial. Ingrained opinions about the nature of hydrogen bonding from across the community made reaching a consensus particularly challenging and ultimately the paper went to over 20 referees before receiving final approval in 2011.

#### Expanding across the periodic table

It was during the course of this collaborative and cross-disciplinary discussion that the team identified the other key problem with IUPAC's existing definition framework – missing terminology. The lack of clarity around these more recently discovered interactions left researchers to



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propose their own definitions for these intermolecular bonds, causing confusion and inconsistency throughout the literature.

The term 'halogen bond', in particular, was widely misused and in 2010 the halogen bond definition project was proposed, with the analogous group 14–16 project initiated shortly after. At a fundamental level, each of these interactions is part of the same wider phenomenon: the uneven distribution of electron density can create a localised electropositive region, even on an electronegative atom. The resulting electrostatic attraction to a nearby nucleophilic region then creates a (typically) weak bond whose identity is determined by the electrophilic atom.

While the changing valency across the periodic table leads to some differences, the underlying principle behind hydrogen, halogen, chalcogen and pnictogen bonds is the same. Resnati's team were keen to ensure consistency across this series of definitions, taking the semantic structure of the new hydrogen bond definition as a model for the rest. 'The extension of the mindset adopted in the new definition of the hydrogen bond to other elements was quite straightforward and reaching a consensus for the halogen and the chalcogen bonds was indeed much easier,' he says.

The recent pnictogen bond definition proved a little more challenging in this regard as the greater valency and more varied nature of the group's elements complicated the definition process. 'In group 15 you move from elements which are typically giving covalent bonds – nitrogen – to elements which are metals – bismuth – so to arrive at a consensus with people with non-minor differences in the concept of their use, bonding and interactions was really tough,' Resnati explains. The project addressed these issues with the final definition:

'[A] weak attractive interaction between an electrophilic region on a pnictogen atom in a molecular entity (wherein the pnictogen is involved in other stronger bonds) and a nucleophilic region in another, or the same, molecular entity.'

This additional complexity meant the team spent a total of six years working on the pnictogen bond definition, almost double the time spent on the halogen and chalcogen bonds. However, this effort has not gone unappreciated by the research community.

### Clarity at last

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Statistics compiled by American Chemical Society (ACS) publications demonstrate the extent to which the chemical community has embraced this new terminology. Following the release of the definition in 2013, halogen bonds were mentioned an average of 73 times a year across all ACS papers, compared with an average of just nine times a year in the 20 years preceding the project's announcement. A similar trend is also emerging for 2019's chalcogen bond, with an average of nine times more annual mentions since the recommendation was published.

Clear and specific terminology also streamlines the process of research itself, providing citable terms for researchers to use in publications. 'It's simplified my life,' says Anthony Cozzolino, a supramolecular chemist at Texas Tech University. 'The definitions help unify the field and give searchable names which, in turn, helps me identify the research that I want to be looking through and target my efforts.' At the same time, the prevalence of secondary bonding interactions across so many different parts of chemistry brings researchers into contact with other research areas which can then guide new strategies drawn from both fields together.

But more widely, the attention surrounding these definitions has shone a light on these interactions as an important and growing area of research. 'Having the IUPAC definitions lends credence to the field that makes it easier to push in new directions,' says Cozzolino. 'In terms of funding, you can show there's precedent for this chemistry which gives weight to grant applications.'

A huge part of the success of these definitions has been the emphasis placed on consensus – a requirement for all IUPAC definitions – and the ACS's Committee on Nomenclature, Terminology, and Symbols (NTS) is just one of the professional bodies invited to offer feedback on the early proposals. 'Definitions help us all speak the same language and align around consistent meanings,' says Clay Harris, strategic initiatives leader for the ACS's NTS committee. 'We value opportunities like this to help ensure that proposals work for chemistry practitioners and our global community of members. These positive interactions support the evolution of common terminology used in the global practice of chemistry.'

Resnati's team are now working on the final definition in the series but the committee expect arriving at a consensus for group 14's tetrel bond will prove the most challenging yet. The central importance of carbon in so many areas of chemistry, and the contrast with the wildly different properties and behaviours of heavier group members such as lead will



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likely make the details of the final definition difficult to establish and it could be years before the final definition is published. 'To arrive at a common opinion shared by chemists with such different backgrounds will be truly challenging but I think that the previous definitions – hydrogen, halogen, chalcogen, pnictogen – are proving that the approach is meaningful,' says Resnati.

Thanks also to Gautam Desiraju, Anthony Legon and Antonio Frontera for their contributions.

Chemistry World, 1 October 2024

<https://chemistryworld.com>

### It all adds up: Study finds forever chemicals are more toxic as mixtures

2024-10-01

A first-of-its-kind study has measured the toxicity of several types of per- and polyfluoroalkyl substances (PFAS), better known as "forever chemicals," when mixed together in the environment and in the human body.

The good news: Most of the tested chemicals' individual cytotoxicity and neurotoxicity levels were relatively low.

The bad news: the chemicals acted together to make the entire mixture toxic.

"Though they are structurally similar, not all forever chemicals are made equal—some are more potent, others less. When mixed, all components contributed to the mixture's cytotoxicity and neurotoxicity," says the study's first-author, Karla Ríos-Bonilla, a chemistry Ph.D. student at the University at Buffalo.

"In the laboratory assays we used in this study, most of the types of PFAS that we tested did not appear to be very toxic when measured individually. However, when you measure an entire sample with multiple PFAS, you see the toxicity," adds study co-author Diana Aga, Ph.D., director of the RENEW Institute, SUNY Distinguished Professor and Henry M. Woodburn Chair in the UB Department of Chemistry.

This research was conducted in collaboration with Beate Escher of the Helmholtz Centre for Environmental Research (UFZ), Leipzig, Germany, where Ríos-Bonilla did the in vitro toxicity experiments in the high-

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throughput screening facility CITEPro. It was published in Environmental Science and Technology.

The study is novel in that it assesses the mixture toxicity of PFAS. These synthetic compounds have been widely used in consumer products—from nonstick pans to makeup—for decades, and they can take hundreds to thousands of years to break down, if ever. They are estimated to be in at least 45% of the nation's drinking water and in the blood of practically every American, and they have been linked to cancer and neurodevelopmental disorders.

Earlier this year, the U.S. Environmental Protection Agency (EPA) issued the first-ever drinking water standards for six kinds of PFAS. However, it is estimated that there are over 15,000 varieties present in the environment. Only a handful of these chemicals have standards and are regulated.

"There are six PFAS that can be regulated because we know a lot about them and their toxicity. Unfortunately, we cannot regulate other forms of PFAS until their toxicities are known," says Aga, who is principal investigator.

"We need to set maximum contamination levels for each PFAS that is proportional to their toxicity. To regulate contaminants, it is crucial to know their relative potencies when they occur as mixtures in the environment along with their predicted environmental concentrations."

#### PFOA and PFOS are major contributors to mixture toxicity

To conduct the study, researchers created their own PFAS mixtures, one that is representative of an average American's blood serum, and the other of surface water samples found in the U.S. Ríos-Bonilla used data from the U.S. Centers for Disease Control and Prevention and from the U.S. Geological Survey to determine the average concentration ratios of PFAS in human blood and in surface water, respectively.

They then tested these mixtures' effects on two cell lines; one that tests for mitochondrial toxicity and oxidative stress and the other for neurotoxicity.

Of the 12 PFAS spiked in the water mixture, perfluorooctanoic acid (PFOA)—commonly used in nonstick pans and firefighting foam—was the most cytotoxic, making up to 42% of the mixture's cytotoxicity.

On the other hand, both PFOA and perfluorooctane sulfonic acid (PFOS) contributed roughly the same cytotoxicity (25%) to the neurotoxicity



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assay, despite both contributing only 10 and 15% to the mixture in terms of concentration, respectively.

The blood mixture had four PFAS present, but PFOA again was the most cytotoxic to both cell lines. Despite its molar contribution being only 29%, PFOA triggered 68% of the cytotoxicity in the cytotoxicity assay, and 38% in the neurotoxicity assay.

Interestingly, when researchers analyzed the toxicity of the extracts from real biosolid samples collected from a municipal wastewater treatment plant, very high toxicities were observed despite the measured low concentrations of PFOA and other PFAS in the sample.

“This means that there are many more PFAS and other chemicals in the biosolids, which have not been identified, that contribute to the toxicity of the extracts observed,” Aga says.

### Synergistically versus additive

One of researchers’ goals was to determine if PFAS acts synergistically. This is when two or more chemicals’ combined effect is greater than the sum effect of the individual chemicals. However, their findings indicate that the effect of PFAS is concentration-additive: this means that an established mixture toxicity prediction model can be used to predict the combined effect of mixtures.

“As up to 12 PFAS in the mixtures acted concentration-additive for cytotoxicity and specific neurotoxicity, it is likely that the thousands of other PFAS that are in commerce and use are also acting in the same manner,” Escher says. “Mixtures pose more of a risk than individual PFAS. As they act and occur in mixtures, they ought to be regulated as mixtures.”

Researchers say the results of this study will also be very useful in assessing the effectiveness of remediation efforts. Breaking down PFAS can sometimes create harmful byproducts that cannot be detected by chemical analysis, so measuring the toxicity of a sample after treatment may be the only way to judge whether a remediation technology is effective.

“Toxicity assays can be a complimentary tool when analytical chemistry doesn’t give you all the answers, especially when the identities of

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contaminants in the mixture are unknown, which is the case in many polluted sites,” Aga says.

Phys Org, 1 October 2024

<https://phys.org>

### Chemists discovered the first new chemical bond in more than a decade

2024-09-25

It is not often that chemists create a new kind of chemical bond, but they have just done it. A covalent bond that relies on a single electron has been made almost a century after it was first proposed.

Takuya Shimajiri at the University of Tokyo and his colleagues have been testing the limits of chemical bonds for years. Previously, they experimented with unusually long and flexible bonds, and now they have taken on an idea first proposed in 1931 by chemist Linus Pauling: a chemical bond formed by just one electron.

All known covalent bonds, where atoms connect by sharing electrons, contain two, four, six or eight electrons – but Pauling theorised a covalent bond could exist with a single electron shared between two atoms. To create this, the researchers used a chemical reaction to remove an electron from an existing two-electron covalent bond between two carbon atoms. They used a large hydrocarbon that has exceptionally long bonds between its carbon atoms, which means it would be energetically costly for an electron from elsewhere in the molecule to replace the one they removed.

Shimajiri says past experiments that attempted such electron subtraction left behind weak bonds which broke too quickly for a definitive chemical analysis. But his team’s molecule remained stable enough they could analyse it with X-rays and several kinds of light. Based on how this radiation bounced off or was absorbed, they determined it had a stable one-electron bond.

“It’s not often that you find a molecule with a new kind of bond,” says Henry Rzepa at Imperial College London. He says the molecule had a total of 278 electrons, so it was a real feat to both remove the correct one and prevent all the others from immediately replacing it. Rzepa says this is a “major discovery” that could lead chemists to create whole new families of molecules.



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Chemists can now study how one-electron covalent bonds may change chemical reactions, says Shimajiri. But he and his colleagues have bigger questions, too.

“We aim to clarify what a covalent bond is – specifically, at what point does a bond qualify as covalent, and at what point does it not? Our goal is to explore a wide range of bonds that have yet to be discovered,” he says.

New Scientist, 25 September 2024

<https://newscientist.com>

### Hydrogel can preserve medications for weeks outside of a fridge

2024-07-17

Many medications must be refrigerated or they lose their effectiveness, but a new method of packing protein-based drugs into a stiff gel could make them last longer at room temperature.

Drugs can break down if they aren't stored properly, which can make them unsafe to use. Exposure to high temperatures, for example, can break the chemical bonds that maintain a drug molecule's shape, disrupting its function. For some drugs, shaking can make their molecules clump together, reducing their efficacy. Matthew Gibson at the University of Manchester in the UK has been working on addressing these challenges for almost 15 years.

He and his colleagues have now developed a method that could make handling protein-based drugs simpler and more practical. He says the new advance came from working with Dave Adams at the University of Glasgow in Scotland, who specialises in making hydrogels. They worked out how to mix proteins with gel ingredients and end up with a stiff white structure that can be loaded into a syringe. In this form, proteins that would usually have to be refrigerated at  $-20^{\circ}\text{C}$  ( $-4^{\circ}\text{F}$ ) withstood temperatures as high as  $50^{\circ}\text{C}$  ( $122^{\circ}\text{F}$ ) and remained functioning under these conditions for up to four weeks.

The hydrogel gets its stiffness from small molecules combined into large chains, which are then broken by applying force. In syringes, pushing down on the plunger breaks the molecular bonds, turning the gel and protein mixture into a liquid. The hydrogel remnants were too big to enter the syringe's needle, so only the drug leaves the syringe.

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The team tested this method with several compounds, including bovine insulin and  $\beta$ -Galactosidase, an enzyme commonly used for gene studies in biology. They also mailed a box filled with containers full of protein-packed hydrogels to themselves and found that the proteins withstood the temperatures and jostling of the journey through the postage system.

Though there are laboratory methods that can keep proteins stable for longer, this approach may be better suited to leave the lab and enter the clinic, says Alex Brogan at King's College London. He says that it would most benefit countries and regions where cold storage is rare and prohibitively expensive. If the new method works with protein-based vaccines, it could make disease prevention more equitable, he says.

Gibson says that he and his team are confident they could make their hydrogel at industrial scales, but they want to conduct more studies on its longevity and safety. While using it with vaccines is on their wish list, in the short term the method could also be used to store, transport and administer semaglutide, a drug used to treat diabetes and obesity.

New Scientist, 17 July 2024

<https://newscientist.com>



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